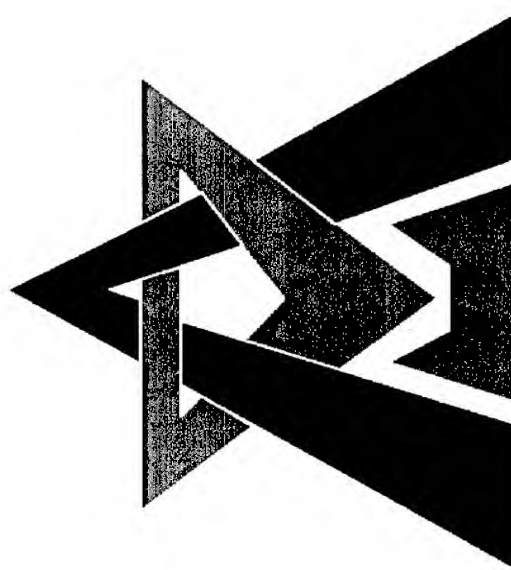


# **Madigan Army Medical Center**

## ***Annual Research Progress Report***



20010221 013

## **Fiscal Year 2000**

Department of Clinical Investigation  
Madigan Army Medical Center  
Tacoma, Washington

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.				
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE 30 September 2000	3. REPORT TYPE AND DATES COVERED Annual 1 October 1999 - 30 September 2000		
4. TITLE AND SUBTITLE Annual Research Progress Report Department of Clinical Investigation		5. FUNDING NUMBERS		
6. AUTHOR(S) Barbara Jones      Troy Patience Paul Froude        Genie Hough				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Department of Clinical Investigation Madigan Army Medical Center Bldg 9040, Fitzsimons Dr, Rm G-15-C2 Tacoma, WA 98431		8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) Clinical Investigation Regulatory Office U.S. Army Medical Center and School (MCCS-GCI) 1608 Stanley Road, Bldg 2268 Fort Sam Houston, TX 78234		10. SPONSORING / MONITORING AGENCY REPORT NUMBER		
11. SUPPLEMENTARY NOTES THE FINDINGS IN THIS REPORT ARE NOT TO BE CONSTRUED AS AN OFFICIAL DEPARTMENT OF THE ARMY POSITION UNLESS SO DESIGNATED BY OTHER AUTHORIZED DOCUMENTS				
12a. DISTRIBUTION / AVAILABILITY STATEMENT APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED		12b. DISTRIBUTION CODE		
13. ABSTRACT (Maximum 200 words)  This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 2000. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 2000. Also included in the report are personnel rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during FY 2000.				
14. SUBJECT TERMS Research protocols, investigators, objectives, progress, technical approach		15. NUMBER OF PAGES 541		16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT UNCLASSIFIED	18. SECURITY CLASSIFICATION OF THIS PAGE UNCLASSIFIED	19. SECURITY CLASSIFICATION OF ABSTRACT UNCLASSIFIED	20. LIMITATION OF ABSTRACT UL	



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**ANNUAL PROGRESS REPORT**

29 SEPTEMBER 2000

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

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FISCAL YEAR 2000  
DEPARTMENT OF CLINICAL INVESTIGATION  
MADIGAN ARMY MEDICAL CENTER  
TACOMA, WASHINGTON 98431

**Introduction**

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

**Acknowledgments**

I would like to take this opportunity to thank Barbara Jones, Troy Patience, Paul Froude and Genie Hough for their effort, in the compilation, preparation, and editing of this publication.

What a year, indeed! The continued expansion of scholarly activity at Madigan Army Medical Center (MAMC) during the last year, with more deployments, and further increased clinical productivity is a tribute to the commitment to excellence of the MAMC community of clinical investigators. Madigan experienced remarkable turnover in graduate medical education programs, house-staff assigned, and certified faculty, yet produced new scholarly activity at historical levels simultaneous with increased patient contacts, care and service. Madigan's Department of Clinical Investigation (DCI) supported 146 new research protocols (29 were oncology group protocols), 74 completed, 31 terminated, 4 suspended and 282 on-going protocols (297 staff, 19 fellow, 63 resident, 9 intern, and 2 external protocols). This represents a 32% increase in new research protocols. The IRB approved protocols involving 372 house-staff, 33 fellows, 139 residents, and 13 interns. DCI has initiated outreach programs to teach the regulatory requirements for ethical conduct of research while providing pre-review and design support for our medical executives seeking to improve the quality of care through a more scientific approach to managed care. The emphasis and priority for Military Unique Medical Readiness in Clinical Investigation continues.

The very important Graduate Medical Education mission at Madigan continues to receive strong support from DCI through leadership in curriculum development, medical education research, and the unique training opportunities available through the departmental programs (i.e. PALS, ATLS, etc.). The following interns, residents, fellows and faculty participated in "Introduction to Clinical Investigation Short Course" (72) and 'Surgical Training Protocols'; i.e., PALS and ATLS (282).

Madigan Research Day 2000 was held 13 April 2000 and offers the best benchmark available for the vigor of multiservice (USA, USAF, USN, USCG) scholarly activity and clinical research at our institution, and within our region. Forty-nine abstracts were submitted and reviewed by subcommittees and 21 selected for podium presentations. In addition, there was a poster session involving 10 presentations. Moderators presented several additional presentations to focus the research efforts in the areas of Military Unique Clinical Investigation, Scientific Approach to Managed Care and Outcome Studies, Medical Education Research, Experimental Design, and Case Reports. The COL Patrick S. Madigan, M.D. Foundation, The Geneva Foundation, and the Henry M. Jackson Foundation supported the effort from conception to execution, including the program brochure and recruitment of judges.

BG Mack C. Hill's opening comments set the stage for the challenge and celebration of scholarly activity at MAMC. Four presentations were awarded Army Achievement Medals in the following areas: **Change of Practice** – *MAJ Tad L. Gerlinger, MC* for "Functional Outcome of Instrumented Posterior Lumbar Interbody Fusion (PLIF) in Active Duty US Servicemen: A Comparison with Nonoperative Management", with mentor: *MAJ Robert Molinari, MC*. **Discovery** – *CPT John J. Mullon, MC* for "The Use of Polymerized Bovine Hemoglobin in a Patient with Severe, Refractory Immune Pancytopenia", with mentor: *LTC George Giacompe, MC*. **Innovation** – *CPT Jeffrey A. Vos, MC* for "Vortex Disaggregation for Flow Cytometry: A Tissue Preserving Method", with mentor: *LTC Mark D. Brissette, MC*. **Interdisciplinary** – *CPT Mark E. McGranahan, MC* for "DoD Newborn Screening: Reengineering Based Upon Risk, Not State Lines", with mentor: *Laura Martin, MD* and *MAJ Wanda Barfield, MC*. The recipient of the Excellence in IRB Service Award (henceforth named in honor of Nancy Whitten) was presented to *COL Dennis R. Beaudoin, MS (Oncologic Pharmacist)*. The BG George J. Brown Mentor's Cube was presented to *COL William O. Walker, MC (Developmental Pediatrician)*. The inaugural Facilitator's Award was presented to *BG Mack C. Hill* and named in his honor.

Madigan Research Day 2001 will be held 27 April 2001 and the Inaugural Western Regional Medical Command Medical Readiness Conference will follow, 28-29 April 2001, thanks to support from the Henry M. Jackson Foundation.

# Unit Summary{ TC "Unit Summary" \1 1 }

## A. Objective:

To provide the facilities and environment to stimulate an interest in clinical and basic investigations within Madigan Army Medical Center and its region.

## B. Technical Approach:

All research, investigational and training activities within the Department of Clinical Investigation are conducted under the guidance of AR 40-7, AR 40-38, AR 70-25, AR 70-18, and HSC Reg 40-23. Careful monitoring of all approved protocols is conducted in order to assure strict compliance with the applicable regulations.

## C. Staffing:

<u>Name</u>	<u>Rank</u>	<u>MOS</u>	<u>Title</u>
Hume, Roderick F., Jr.	COL	60J9A	Chief, DCI
Norlund, Lewis L.	MAJ	75C64	Asst Chief, DCI; Chief, Lab Animal Resources Service
Rossignol, Todd M.	CPT	71B67	Chief, Research Operations Service
Carpenter, Steven W.	SFC	91T4H	NCOIC
Chapman, Tiffany D.	SSG	91T30	Senior Animal Care Specialist
Sanchez, Michael J.	SPC	91T10	Animal Care Specialist
Blake, Terri L.	GS13	0601	Research General Health Scientist
Matej, Louis A.	GS11	0644	Medical Technologist
Wright, James R.	GS11	0644	Medical Technologist
DeHart, Mary Jo	GS11	0644	Medical Technologist
Bullock, Jeff M.	GS11	0644	Medical Technologist
Patience, Troy H.	GS09	1530	Statistician (Medicine)
Kaeo, Curtis K.*	WG07	4749	Maintenance Worker
Spahn-Bridges, Shelley L.	WG05	5048	Animal Caretaker
Jones, Barbara A.	GS07	0301	Research Protocol Specialist
Hough, Eugenia R.	GS06	0318	Secretary/Steno
Froude, Paul	GS05	0303	Clinical Research Associate

\* Deceased

## Staffing Summary:

	Authorized	Required	Assigned
Officers -	4	10	3
Civilians -	8	12	10
Enlisted -	8	12	3

#### **D. Research Funding**

Civilian Payroll	\$ 622,000	
Incentive Awards	\$ 1,300	
Operations	\$ 90,200	
Funds for training protocols	\$ 3,770	
CEEP	\$ 6,600	
TDY	\$ 4,600	
TDY for researchers to present	\$ 40,000	
Print/Publications	\$ 3,000	
Contracts	\$ 9,000	
<b>OMA Total:</b>		<b>\$ 780,470 (total)</b>

#### **Grants Federal (includes grants from all intermediaries)**

Air Force (MFM)	\$ 12,320
Henry M. Jackson Foundation	\$ 32,266
The Geneva Foundation	\$ 227,216

#### **Grants Nonfederal: (includes grants from all intermediaries)**

CRDA	\$ 44,671
Henry M. Jackson Foundation	\$ 62,975
The Geneva Foundation (all CRDA)	\$ 78,050

<b>Grants (GRAND TOTAL):</b>	<b>\$ 457,498 (total)</b>
------------------------------	---------------------------

MEDCASE:	\$ 0	
Military Payroll:	\$ 479,000	
<b>Non-OMA Total:</b>		<b>\$ 479,000 (total)</b>

**\$ 1,716,968 (total)**



#### **D. Progress**

During FY 2000, there were 391 active protocols that received administrative and/or technical support during the year. Of these, 282 are presently ongoing, 4 are in a suspended status, 74 were completed, and 31 were terminated. The principal investigator distribution was as follows: 297 staff protocols (includes 138 group oncology protocols), 63 resident protocols, 19 fellow protocols, 9 intern protocols, 1 ROTC protocol and 1 Weed Army Community Hospital protocol. There were 146 new protocols, 29 of which were Oncology Group protocols.

There were 69 publications in nationally recognized journals and 43 presentations at regional or national medical association meetings.

#### **E. Fellowship/Residency Program Support**

**Fellowship/Residency programs supported by DCI:** 21 residencies and 5 fellowships, they are: *Residencies:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Occupational Therapy, Ophthalmology, Oral and Maxillofacial Surgery, Orthopaedic Surgery, Otolaryngology, Pathology, Pediatrics, Pediatric Psychology, Pharmacy, Physician Assistance Program (Emergency Medicine & Orthopaedics), Podiatry, Preventive Medicine (Public Health), Radiology, Transitional Year, and Urology.

*Fellowships:* Developmental Pediatrics, Faculty Development (Family Practice), Geriatrics, Maternal-Fetal Medicine, and Urogynecology.

114 protocols involving 139 residents

83 protocols involving 33 fellows

#### **Other training programs supported by DCI:**

Training protocols: Department of Surgery: 4

Department of Emergency Medicine: 2

Department of Obstetrics/Gynecology: 1

Ranger Battalion: 1

## **G. Committee Members**

### **Clinical Investigation Committee**

**COL Roderick F. Hume, Jr., MC**  
**Chairman**

**Chief or delegated representative of:**

**Department of Emergency Medicine**  
**Department of Family Practice**  
**Department of Medicine**  
**Department of Nursing**  
**Department of OB/GYN**  
**Department of Pathology**  
**Department of Pediatrics**  
**Department of Radiology**  
**Department of Surgery**  
**Pharmacy Service**  
**Physical Medicine & Rehabilitation Service**  
**Department of Clinical Investigation**  
**Biochemistry Section, DCI**  
**Lab Animal and Resources Service, DCI**  
**Medical Statistician, DCI**  
**Microbiology Section, DCI**  
**Research Administration Service, DCI**

**F. Committee Members (cont'd)**

**Human Use Committee**  
COL Roderick F. Hume, Jr., MC  
Chairman

Chief or delegated representative of:

Department of Nursing  
Department of Pediatrics  
Department of Radiology  
Department of Ministry and Pastoral Care  
Department of Clinical Investigation  
Pharmacy Service  
Social Work Service  
Center Judge Advocate  
Non-institutional Member

**Animal Use Committee**  
COL Roderick F. Hume, Jr., MC  
Chairman

Chief or delegated representative of:

Department of Nursing  
Northwest Veterinary Support Service Area  
Non-institutional Member  
Research Operations Service, DCI  
Lab Animal & Surgery Service, DCI  
NCOIC, Lab Animal & Resources Service, DCI



**Madigan Research Day**  
*3<sup>rd</sup> Annual Meeting Proceedings*

13 April 2000, Letterman Auditorium,  
Madigan Army Medical Center  
Fort Lewis, Washington

**GOALS**

The goals for this program are threefold: Celebrate the Exceptional Scope of Scholarly Activities at MAMC, Incite Enthusiasm (for further studies, grant submissions, and publications at MAMC), and Attract Grant Support for MAMC.

## AWARDS

Four presentations are nominated for awards (Army Achievement Medal): Innovation, Interdisciplinary, Discovery, and Change In Practice.

### FIRST ANNUAL MADIGAN RESEARCH DAY AWARDS

Each of the 66 submissions was eligible for the 4 awards. The awards were selected by judges scoring for the best in each category. The First Annual MRD winners were: **Change of Practice** - "The Effect of Loaded Foot Marching vs Running on Injury, Fitness, and Performance In US Army Light Infantry Soldiers" presented by CPT Dan C. Norvell, SP; **Discovery** - "Purple Toes" presented by CPT Brian P. Mulhall, MC; **Innovation** - "Tracheal Mucosal Healing in Response to Moderate Mucosal Injury Induced by Expandable Metallic Stents" presented by LCDR Keith Ulnick, MC USN; **Interdisciplinary** - "The Routine Pregnancy Process: Framework for Clinical Pathway Genesis" presented by 1LT Cristen Brandsma, AN.

### SECOND ANNUAL MADIGAN RESEARCH DAY AWARDS

Each of the 55 submissions was eligible for the 4 awards. The awards were selected by judges scoring for the best in each category. The winners were: **Change of Practice** - CPT Laura L. Feider, AN for "Risk Factors for Nosocomial Pneumonia in the Intensive Care Unit". Mentor: Mary McCarthy, RN, MN, Critical Care Nursing, **Discovery** - CPT Samuel S. Jang, MC for "Targeting Hearing Loss Prevention at the High Risk Populations". Mentor: LTC (P) Jeffrey D. Gunzenhauser, MC, Preventive Medicine. **Innovation** - CPT Eric Shry, MC for "Utility of Echocardiography in Asymptomatic Active Duty Service Members with Heart Murmur". Mentor: MAJ Maureen Arendt, MC, Cardiology/Internal Medicine. **Interdisciplinary** - MAJ Brian Harrington, MC for "Evaluation of Clinical Standards Implementation at Madigan". Mentor: COL Joseph Yetter, MC, Family Practice.

### THIRD ANNUAL MADIGAN RESEARCH DAY AWARDS

Each of the 49 submissions was eligible for the 4 awards. The awards were selected by judges scoring for the best in each category. The winners were: **Change of Practice** - MAJ Tad L. Gerlinger, MC for "Functional Outcome of Instrumented Posterior Lumbar Interbody Fusion (PLIF) in Active Duty US Servicemen: A Comparison with Nonoperative Management". Mentor: MAJ Robert Molinari, MC. **Discovery** - CPT John J. Mullan, MC for "The Use of Polymerized Bovine Hemoglobin in a Patient with Severe, Refractory Immune Pancytopenia". Mentor: LTC George Giacoppe, MC. **Innovation** - CPT Jeffrey A. Vos, MC for "Vortex Disaggregation for Flow Cytometry: A Tissue Preserving Method". Mentor: LTC Mark D. Brissette, MC. **Interdisciplinary** - CPT Mark E. McGranahan, MC for "DoD Newborn Screening: Reengineering Based Upon Risk, Not State Lines". Mentor: Laura Martin, MD and MAJ Wanda Barfield, MC.

**SESSION 1:**  
**Military Unique Clinical Investigation**  
**Moderator: LTC C. Ray Dotson, MS**

The care and welfare of our soldiers, airmen, and sailors is the central concern of our military research efforts. The essential process required to preserve and maintain the fighting strength (...salvage our manpower for the unique military missions...) is to anticipate the threat, solve the problems, and work through the medical challenges that the deployed soldier may encounter. At the Joint Services Graduate Medical Education Selection Board, Secretary Martin coined the term 'Military Unique Clinical Investigation'. Subsequently, the Surgeon General from each of the DOD services stated that more military unique curriculum development and more military unique research were needed. This message was clear and anticipated at Fort Lewis by both Madigan Army Medical Center (MAMC) and I Corps leadership. There is already an existing tradition of collaborative militarily relevant clinical investigation efforts between MAMC and I Corps and this remains a fundamental element of future plans at this installation.

**Title:** Female Soldier Readiness: A Leader's Guide - Utility Validation Survey

**Presenter:** CPT David J. Phillips, EN

**Department:** Department of Clinical Investigation

**Mentor:** LTC Peter Nielsen, MC and COL Robert E. Ricks, MC

**Abstract:**

**Objective:** The current study evaluates the utility of our ongoing educational initiative for Female Soldier Readiness. This initiative has developed a handbook for small unit leaders to facilitate the optimal personnel management for female soldiers. This survey seeks to answer two questions: Where in the leadership development process should the guide first be introduced (PLDC, ANCOC, OBC, OAC, etc), and what level of leadership has the most critical need for the information contained in the guide.

**Instrument:** The Leader's Guide covers the areas which usually leave the leader guessing, such as pregnancy counseling and profiles, exercise during pregnancy, unintended pregnancy prevention programs, and field needs of female soldiers. The handbook and the resources within are meant to help the leader integrate this specialized knowledge into the planning process to eliminate potential problems before they arise.

**Experience:** Primary development of the Guide began in 1995. Since then, it has been staffed through the OG Consultants to OTSG, presented to AFD/ACOG 1996/97/99, briefed at JSGMESG 98, staffed through CG AMEDD C&S leading to inclusion of the KMN, and staffed through the SGS, I Corps, Fort Lewis. The phased fielding trials involved distribution of the Guide and follow-up survey to seven units on Fort Lewis: 1st Brigade, 25th Infantry Division; 3rd Brigade 2nd Infantry Division; 1st Military Police Brigade; 201st Military Intelligence Brigade; 555 Engineer Group; 62nd Medical Group; and Troop Medical Command, MAMC.

**Conclusion:** Military Unique Clinical Investigation through interdisciplinary collaboration at Fort Lewis between I Corps and MAMC works. Further integration of the Guide will be implemented under the auspices of CHPPM-West. Widespread utilization of this tool, and web-based access through the AMEDD C&S KMN should provide the leader critical information in order to maintain the fighting force.

**Title:** The Prevalence of Hepatitis A in ROTC Cadets

**Presenter:** CPT Marten Duncan, MC

**Department:** Department of Medicine/Gastroenterology Service

**Mentor:** MAJ William Hirota, MC and COL Amy Tsuchida, MC

**Abstract:**

**Background:** Hepatitis A is a major cause of soldier morbidity. Previously the US military relied upon predeployment prophylaxis with immunoglobulin conferring only short-term immunity. A formalin inactivated vaccine is now available providing at least six to ten years of immunity. In 1996 the Department of Defense (DoD) mandated that active duty personnel be immunized with this vaccine. According to the NHANES III study the overall seroprevalence of hepatitis A is 38%. In adults aged 18-32 the prevalence is 18%. A Dutch military study suggested that the threshold for prescreening prior to vaccination needed to confer a cost-savings was greater than 20%. No similar data is available for US Army recruits to help guide vaccination practices in an era where cost containment is paramount.

**Objective:** To determine the seroprevalence of prior hepatitis A infection in ROTC cadets. Validate the current DoD policy of hepatitis A vaccination in newly enrolled troops without prescreening for previously acquired immunity. Two strategies were compared: (1) vaccination without prescreening, (2) prescreen and vaccinate only those without evidence of prior infection.

**Methods:** This is a prospective cohort study in which 1330 ROTC cadets were enrolled to estimate the seroprevalence of hepatitis A in officer recruits. Serologic samples were tested with a standard ELISA. Biographical data was collected from the ROTC command including age, gender, race, and state origin as defined by college location. Costs were calculated using a range of prevalences to demonstrate differences between the two vaccination strategies.

**Results:** One hundred and seventy seven cadets (13.3%) had serologic evidence of past hepatitis A infection. There were higher prevalence rates in minority populations with a rate of 17% ( $P < 0.05$ ). A cost analysis revealed that prescreening for hepatitis A prior to vaccination was cost saving if the prevalence was greater than 20%.

**Conclusion:** The seroprevalence of hepatitis A in ROTC cadets is 13.3%. Prescreening for hepatitis A prior to vaccination is only cost saving when the prevalence is greater than 20%. This finding supports the current DOD strategy to provide this vaccination to all soldiers without prescreening.

**Title:** Prevention of Unintended Pregnancy Among Army Women

**Presenter:** LTC Diane M. Flynn, MC

**Department:** Department of Family Practice

**Mentor:** COL Jeffrey Clark, MC

**Abstract:**

**Objective:** Over half of soldiers who present for prenatal care report that their pregnancies are unintended. We describe the preliminary results of a pilot intervention to decrease unintended pregnancy in military women.

**Design:** Retrospective cohort study

**Setting and Participants:** All 383 female soldiers who presented for prenatal care at Madigan Army Medical Center during the one-year period, December 1997 - December 1998.

**Intervention:** Facilitated access to contraceptive services and a 3-hour interactive class on reproductive health. Military units were selected for the intervention non-randomly, in deference to post command opposition to randomization in this study.

**Outcome Measures:** Comparison of risk of unintended pregnancy in pregnant women who received the intervention with those who did not.

**Statistical Tests Used:** Relative risk and 95% confidence interval.

**Results:** 363 out of 383 female soldiers (95%) who presented for prenatal care indicated the intendedness of their pregnancies. The risk of unintended pregnancy was 0.57 in the 20 women who participated in the intervention prior to becoming pregnant and 0.54 in the 343 women who did not participate (relative risk 1.1, 95% confidence interval: 0.99,1.24).

**Conclusions:** The unintended pregnancy prevention program did not result in a lower risk of pregnancy in the small number of women who presented for prenatal care after receiving the intervention. Possible explanations for lack of a protective effect include ineffectiveness of the intervention, insufficient sample size to detect an effect, or a higher baseline risk of unintended pregnancy among the intervention group. Limitations of this analysis include nonrandom selection of program participants and non-inclusion of most women whose pregnancies ended in spontaneous or induced abortion. Future analysis will include comparison of self-reported unintended pregnancy rates in 334 women who participated in the intervention with 666 women who did not. This pilot study provides the foundation for a large-scale randomized clinical trial of this intervention.

**Title:** Functional Outcome of Instrumented Posterior Lumbar Interbody Fusion (PLIF) In Active Duty U.S. Servicemen: A Comparison with Nonoperative Management

**Presenter:** MAJ Tad Gerlinger, MC

**Department:** Department of Surgery, Orthopedics Service

**Mentor:** MAJ Robert Molinari, MC

**Abstract:**

**Purpose:** To evaluate the effectiveness of instrumented PLIF procedures in active duty military personnel with chronic back pain and single level lumbar disc degeneration.

**Materials:** 25 consecutive U.S. active duty military servicemen with a history of greater than one year of chronic low back pain symptoms, and MRI evidence of single level lumbar disc degeneration, either isolated DDD (n=13) or low-grade isthmic spondylolisthesis (n=12), were referred to the same surgeon (RVM) at a military spine specialty clinic for treatment. All of these servicemen had a history of duty restriction profiles for back pain totaling 3 months or greater during the year prior to referral. 15 servicemen were treated operatively with instrumented PLIF using autogenous iliac crest bone graft, non-threaded interbody cages (Brantigan or Harms) and a 4 - pedicle screw/rod construct. A concomitant posterior-lateral fusion was performed in all 15 cases. 10 servicemen were treated nonoperatively with spinal extensor muscle strengthening exercise, medications, and restricted duty. The average follow-up time was one year (range 3 - 19 months). All servicemen completed a validated functional outcome questionnaire with emphasis on levels of pre and post treatment function, pain and satisfaction.

**Results:** 5/10 (50%) of the servicemen managed nonoperatively underwent MEB for disability, 3/10 (30%) remained on permanent duty restriction profiles, and 2/10 (2%) returned to full, unrestricted military duty. Only 4/10 nonoperatively managed soldiers (40%) were able to complete the standard military PT test. In the PLIF group, 12/15 soldiers (80%) were able to return to full, unrestricted military duty, 3/15 (20%) remained on permanent restrictive military duty profiles, and 0/15 (0%) underwent MEB for disability. 12/15 (80%) of the PLIF group completed the standard military physical training test. Of the soldiers who were able to complete the PT test (n=16), there were no significant differences between the last completed PT test prior to treatment and the post treatment PT test scores in either group. However, scores for patient assessed post-treatment pain, function and satisfaction were higher in the PLIF group.

**Conclusions:** Instrumented PLIF surgery performed in active duty U.S. servicemen with chronic low back pain and single level lumbar disc degeneration results in high rate of return to full military duty. Servicemen treated with this technique are less likely to receive a back pain disability discharge or a permanent physical limitation profile when compared to servicemen



treated nonoperatively. Outcomes with respect to pain, function, and satisfaction are excellent in those servicemen who are able to return to unrestricted duty.

**Title:** A Critical Review of the Army Medical Board System

**Presenter:** CPT Clinton Schreckhise, MS

**Department:** Hospital Administrator's Masters Program

**Mentor:** COL Van R. Booth, MS

**Abstract:**

To support a physically and mentally prepared Army, the Army medical infrastructure evaluates and processes soldiers as necessary through the Physical Disability Evaluation System. This study examines two critical questions: Where are the inefficiencies in the process and how can the Army approach the mission differently to reduce processing times?

Retrospective data, consisting of 200 MEB cases, provided the basis for examining the process as implemented at Madigan Army Medical Center (MAMC), Fort Lewis, Washington. The researcher used stepwise linear regression analysis to determine relationships among variables and the overall process. This statistical method revealed where the greatest impediments lie for processing cases. Comparisons with the Air Force and Navy programs uncovered suggestions for improving the program.

The research effort relied upon existing data maintained by MAMC, interviews with various service representatives, and SPSS software for analyzing the data. Results of the research indicate that the average MEB processing time at MAMC is approximately 157 days. This time spans from notification of intent to start a MEB until completion. Two steps in the process consume 92.5% of the time: 1) the delivery of care ( $p < 0.001$ ) and 2) preparation of the MEB narrative summary ( $p < 0.001$ ). By comparison, the two sister services accomplish the same MEB tasks much quicker. The Air Force performs best, completing MEBs within 21 days on average.

Study conclusions include considering the Air Force approach and adopting processes as allowable considering mission requirements. Also, findings indicate an error in how the Army counts processing days based on the automated tracking tool used. Modifications to the software, or by-hand calculations, are necessary to accurately report processing times. Finally, the Army should reconsider addressing all medical complaints rather than simply focusing on conditions considered disqualifying for service.

**SESSION 2:**  
**Outcome Study (Scientific Approach to Managed Care)**  
**Moderator: Nancy Newth Greenfield, RN, MS**

Managed care is a concept and a framework for health care delivery. Maturation of managed care systems is occurring across the country and at Madigan. This framework, when actualized at Madigan, is a dynamic and evolving system. Our managed care system is incredibly complex, with overlapping and matrixed components. Some macro components of a managed care system are the benefits package and the "rules of engagement", such as how one enrolls, how care is accessed, and how an appointment is made. In addition, more cryptic components include customer service, satisfaction of the beneficiary and the providers, information availability and exchange, internal measurement of processes, priority setting for resource allocation and internal interfaces or handoffs. These cryptic components are governed and influenced by the "culture" of the organization.

Organizational culture includes the openness of the system, communication style and expectation, self-exploration and self-analysis of the system itself, and the education and mentoring of the participants within the system. Why do some managed care systems thrive and others fail? That is where the "science" comes in.

Madigan has enjoyed an evolving culture carefully mentored to be inclusive of concepts of total quality management and continuous quality improvement, embraced by Madigan as we continue our journey into the development of our managed care system. The growth of managed care and science is intimately linked. How do we know what the "right thing, at the right time" is? How do cost factors influence the delivery of health care? Does decreased variability in health care delivery make a difference? How? Do clinical pathways improve outcomes?

The study of macro and micro components of our managed care system is a part of our culture, reflected in the proceedings of today. Mentoring of our staff to study our systems, resources to support that system, reward for the efforts and outcomes, information available to proceed, are all part of the Madigan culture, culminating in this session, the scientific approach to managed care.

**Title:** The Alaska Federal Health Care Partnership: An Approach to Improving the U.S. Coast Guard Health Care System Through Interagency Support

**Presenter:** LT Mark Everett, USCG, CAAMA

**Department:** Hospital Administrator's Masters Program

**Mentor:** LTC Margaret Rivera, MS

**Abstract:**

TRICARE Prime Remote (TPR) was designed to address deficiencies in health care benefits for service members assigned to remote locations. Through involvement in the Alaska Federal Health Care Partnership (AFHCP), the four U.S. Coast Guard (USCG) clinics in Alaska have reduced costs, improved the quality of health care, and overcome some access problems in spite of their geographic isolation. In the wake of the implementation of TRICARE Prime Remote, should the USCG pursue similar interagency relationships to support its geographically remote beneficiaries outside Alaska?

There are three types of AFHCP initiatives: joint contracting, revenue recapture, and use of technology. This retrospective, descriptive business case study used a cost benefit analysis method called the "balance-sheet" approach to tabulate who bore the costs and who reaped the benefits from these AFHCP initiatives at Alaskan USCG clinics in Fiscal Years 1997 through 1999. The balance-sheet approach facilitated evaluation of quantifiable and unquantifiable changes in cost, quality, and access factors as a basis for program evaluation. The AFHCP initiatives found most beneficial to Alaskan USCG clinics and their constituencies were joint contracting for health care services and in-clinic visiting specialist programs (revenue recapture). Though only begun in Fiscal Year 1999, the use of teleradiology technology will likely prove beneficial as well.

The USCG Health Services Program has no formal strategic plan. Its business strategy has been, by default, overwhelmingly opportunistic and reactive in nature. To the extent that approach will remain the business strategy, the USCG should continue to aggressively pursue interagency relationships that support any and all USCG clinics and beneficiaries. Areas for primary focus should be remote clinics responsible for beneficiaries assigned to locales where TPR has been implemented.

**Title:** Outcomes of a Mandated HMG CO A Reductase Inhibitor Conversion at Madigan Army Medical Center

**Presenter:** MAJ Emery Spaar, MS

**Department:** Department of Pharmacy

**Mentor:** COL Dennis R. Beaudoin, MS

**Abstract:**

**Background:** The Department of Defense (DoD) Pharmacoeconomic Committee in order to reduce costs and improve uniformity of care has directed that only two HMG Co A Reductase Inhibitors (statins) be on formulary within the Military Healthcare System. All DoD beneficiaries will be converted to either cerivastatin or simvastatin by 1 April 2000. Between 1 October 1999 and 31 January 2000, utilizing an approved conversion table and therapeutic substitution process, of 2,473 patients previously on other statins prescribed by in house prescribers, 1,503 were converted to the approved agents as mandated. We will report on the conversion process, implemented drug conversion table, educational marketing tools, and resultant outcomes on converted patients. The retrospective analysis of outcomes measured included cost avoidance, adverse reactions, and efficacy of new agents before and after conversion.

**Purpose:** To evaluate the efficacy and cost avoidance of DoD Contract Statins.

**Methods:** Combine data from the following three databases Composite Health Care System (CHCS), Ambulatory Data System (ADS), and Corporate Information System (CIS) to create a relational database.

**Results:** Pending

**Conclusions:** Pending

**Title:** Can a Strategy be Developed for More Cost-Effective Ordering of Cardiac Injury Marker (CIM) tests?

**Presenter:** CPT Jude M. Abadie, MC

**Department:** Department of Pathology

**Mentor:** LTC Jerome B. Myers, MC

**Abstract:**

**Background:** While recent studies published on CIMs (TnI, CK-panel, CKMB, and myoglobin) agree that TnI is the most specific test for diagnosing acute myocardial infarction (AMI), agreement on ordering criteria is ambiguous. Some studies report that TnI detection time is equivalent to that of CKMB; CKMB is the best choice for assessing AMI and that TnI is only needed for specific confirmation, late presentation, or in assessing risk. Some say that TnI tests should completely replace testing for all other markers. Other studies cannot agree on specific CIM combinations needed to accurately assess AMI. Consequently, the ordering of CIM assays at Madigan Army Medical Center (MAMC) can be non-specific, ambiguous, and therefore quite costly.

**Purpose:** Design a cost-effective strategy and outline criteria for ordering CIM assays by comparing MAMC CIM testing patterns to guidelines described in recently published prospective hospital studies investigating CIM.

**Methods:** Retrospective study analyzing over 17,500 CIM testing patterns performed on more than 3000 patients during the 1999 calendar year (99CY) at MAMC.

**Results:** The MAMC chemistry laboratory spent over \$115,000.00 during the 99CY for the measurement of CIM. These represent less than 5% of the tests performed in the chemistry section; however, it consumes more than 20% of the supply budget. This disproportionate expenditure is due to numerous dissimilar voluminous ordering patterns.

**Conclusions:** Proper assessment of CIM can lead to rapid and precise diagnosis of AMI and subsequently save lives. Based on our CIM testing analysis and on reviews of several prospective studies, this retrospective study outlines a specific strategy to make CIM testing more cost-effective at MAMC.

**Title:** 14C-Urea Breath Test: A Breath of Fresh Air for an Old Problem

**Presenter:** MAJ Stacia Spridgen, MS

**Department:** Department of Pharmacy

**Mentor:** COL Dennis R. Beaudoin, MS

**Abstract:**

*Helicobacter pylori* is associated with many gastrointestinal disorders, ranging from chronic gastritis to gastric lymphoma and adenocarcinoma. It is most widely known as the cause of duodenal and gastric ulcers. Approximately 1 in 6 individuals with this infection develops a peptic ulcer; therefore, large numbers of people are at risk.

There are several methods, which can be used to diagnose whether a patient is infected with *H. pylori*. They differ in being invasive or non-invasive, simple or difficult, inexpensive or expensive. Compare to other diagnostic conventions, the breath test has the important advantage of being both non-invasive and able to confirm *H. pylori* eradication about one month after antimicrobial treatment is completed.

Until recently, serology and endoscopy were the only methods employed by Madigan's physicians to assess for active infection and eradication of *H. pylori*. The Nuclear Medicine clinic began performing the breath test in April 1999 under the direction and guidance of the Nuclear Pharmacist. Numerous clinical studies have shown the effectiveness of antimicrobial regimens for treating positive *H. pylori* patients and the importance for testing for eradication.

With the budget concerns and increased drug resistance constantly looming over our heads, this test could prevent unnecessary prescribing of antimicrobial therapy for *H. pylori* patients based on inaccurate serology results. Also, some patients who have been on chronic treatment with PPIs and H2 blockers may need to be tested and worked up for *H. pylori*. A percentage of this population if positive for *H. pylori* can be challenged with a course of antimicrobials; retested with the 14C-urea breath test, and possibly taken off chronic PPIs/H2 blockers.

With accurate retest data, the following parameters could be monitored more effectively: the number of patients being treated for *H. pylori* infections and the regimens being used, the number of *H. pylori* eradication failures and the failing regimens, and emerging patterns of resistance for this infectious disease.

**Title:** DoD Newborn Screening: Genetic Risk Should not be Limited by State Lines

**Presenter:** CPT Mark McGranahan, MC

**Department:** Department of Pediatrics/Medical Genetics

**Mentor:** Laura Martin, MD and MAJ Wanda Barfield, MC

**Abstract:**

**Introduction:** Military newborn metabolic screening is currently limited by state-based decisions.

**Objective:** We hypothesize that a revision in current newborn screening practices in the DoD will capture the ethnic diversity of genetic risks for metabolic and endocrine diseases seen in our population.

**Methods:** We evaluated all U.S. Military Health System eligible births for 1996 (n= 67,894). We then analyzed data regarding location of birth, race, gender and compiled information regarding metabolic and endocrinologic disorders screened in newborns at DoD Regional Medical Centers. We cataloged all state metabolic screening laboratories utilized and the cost of each screen. We then selected acceptable disorders for newborn screening based on ethnic distribution of the DoD population, reliability of testing method, and evidence-based research on the effectiveness of early detection and therapy.

**Results:** We found that DoD births differed from the civilian sector in ethnicity but not in gender. DoD populations had a greater percentage of African-American, White, and Hispanic births. We found that all DoD neonates received screening for hypothyroidism, and phenylketonuria. All other tests were screened at the discretion of each state. We also found no relationship between the cost of screening and the number of conditions screened.

**Conclusions:** Based on these preliminary findings, we recommend that DoD newborn screening be based on ethnic distribution and genetic risk, not state or region of birth. Disorders that should be screened include Biotinidase Deficiency, Congenital Adrenal Hyperplasia, Galactosemia, Amino Acid Disorders (MSUD and PKU) Congenital Hypothyroidism, Hemoglobinopathies, Cystic Fibrosis, Medium Chain Acyl-Co A Dehydrogenase Deficiency and Glutaric Acidemia type 1. We devised an algorithm for newborn screening in the DoD to include term and premature newborns, which encompasses early discharge, family PCS moves, and DoD eligibility changes. Finally, we recommend benchmark qualities of an appropriate laboratory facility, which include centrality, extensive experience, administrative support, genetic consultation, and web-based reporting systems. If cost-effective, the program should be disseminated throughout the DoD.

**Session 3:**  
**Medical Education Research**  
**Moderator: COL Patrick Kelly, MC**

Medical Education Research seeks to determine the best method to teach, to instruct, in order to optimize learning. How do we take the lead in learning? Curriculum development is only the beginning. How do you impart enthusiasm for life long learning in our students? What is the outcome by which we measure our success? MAMC teaches teachers, cultivates mentors, and empowers the investigator to question our educational process. Medical Education Research is truly force amplification by enhancing our future medical readiness.

**Title:** A comparison of the values and attitudes towards work of active duty soldiers and civilians under age thirty-five with those age thirty-five and over at Madigan Army Medical Center

**Presenter:** Carol A Nichols, M.Ed., BSN, RN

**Department:** Department of Nursing, Consolidated Education

**Mentor:** COL Melissa Forsythe, AN

**Abstract:**

Approximately 50 million people in the United States are approaching or are in their 20s. Commonly referred to as Generation -X, their work values and attitudes differ greatly from older workers. This study was to determine if a heightened awareness of the differences in work values and attitudes between younger and older workers would result in a modification of teaching strategies. A work values survey of a convenience sample of 160 active duty soldiers and civilian staff in an Army medical center, along with instructor and trainer interviews, indicated that work values differ between older and younger workers. Descriptive data and instructor interviews indicated that younger workers in a military setting had even higher work values than younger workers depicted in the literature. Interviews revealed young students performed very competently when traditional instructional methods were employed, especially hands-on and lecture format, as long as lectures were interactive and less than 30 minutes per topic area. Further study is needed to determine if healthcare workers in the military have significantly higher work values and attitudes than their non-military cohorts, and how these values affect the methods employed for education and training.

**Title:** Mentoring for the New Millennium: Enhanced Scholarly Activity, Professional Development, and Personal Satisfaction for Future Academics through the Successful Implementation of a Mentor System

**Presenter:** COL William O. Walker, MC

**Department:** Department of Pediatrics, Developmental Pediatrics

**Abstract:**

In response to the new guidelines from the American Board of Obstetrics and Gynecology Maternal-Fetal Medicine programs were mandated to convert from two-year programs to a three-year program. This was not simply adding another year to the training obligation. The major emphasis was a significant transformation from practice to research with at least 18 months dedicated to scholarly activity. The stated goals included an increase in the level of academic and research sophistication and performance of the graduating Maternal-Fetal Medicine Subspecialist. We chose to view the new three-year format as a call for re-engineering existing practices into a faculty development and clinical investigator track. It quickly became apparent that Mentoring is the key to success. How do you teach mentors? How do you provide the increased faculty and fellow time during downsizing? We became quite proactive in resource sharing and partnerships

within our institution. We adopted curriculum from the Faculty Development Fellowship received the support of Graduate Medical Education for supplemental education, and developed a Medical Education Research Program. The most important element is the adoption of the Mentor System. Each fellow has a clinical mentor and a research mentor. We established timelines for completion of research objectives based upon the Guide to Learning and realistic time management. Research activity acquired the same priority as excellent patient care.

Fellows take introductory courses in Molecular Genetics Laboratory Methods, Clinical Investigation and Study Design, and Research Protocol Submission. Feedback is frequent, face-to-face and documented quarterly. The purpose is to give the fellow the resources, time and mentoring to accomplish their goals. These same methods were applied to military and professional development throughout our entire program. We have sustained a remarkable increase in scholarly activity with more approved research protocols, funding, presentations and publications than in the previous program years. Personal satisfaction and career goal achievements are up. It does not appear to be the number of fellows or faculty which is most important, but rather a change in attitude, priorities, and direction. The ABOG Board Directives had it right. We must sustain the mentoring process as core.

**Title:** Localization of Lung Nodules: Technique and Preliminary Results of Coil-suture Localization System Prior to Video-assisted Thoracoscopic Surgery (VATS)

**Presenter:** CPT John P. Reinschmidt, MC

**Department:** Department of Radiology

**Mentor:** Sean P. Murray, MC

**Abstract:**

**PURPOSE:** Small pulmonary nodules remain difficult to biopsy. We describe a new pulmonary nodule localization technique, and describe preliminary human safety and efficacy.

**METHOD/MATERIALS:** A coil-suture lung nodule method was developed ex-vivo for use in combination with video-assisted thoracoscopic surgical resection. Following institutional human-use approval, seven patients presenting with small pulmonary nodules were enrolled. CT was used to place the coil-suture combination. Size, depth to pleura, location and number of nodules were recorded. Success was determined by adherence of coil-suture combination to lung parenchyma during VATS. Factors affecting surgical success, length of procedure and complications are described. Surgeon acceptance and patient tolerance are described.

**RESULTS:** The coil-suture device was successful at anchoring the nodule and lung parenchyma in all five patients. Mean nodule size was 7.6 mm (range 3 to 10mm) with depth to pleura of 12.7mm (range 4 to 31mm) respectively. Single nodules were noted in five patients, two and three nodules in the remaining two patients. Histology revealed benign diagnosis in five patients, and malignant in two patients. Procedure lengths were less than one hour in six cases. Mean time interval between CT nodule localization and VATS was 229-min (range 88-min to 553-min). Three cases were converted to open thoracotomy, two due to failure of VATS due to adherent lung, and the third due to error in coil-suture placement. Patients tolerated the procedure well, and surgeons uniformly accepted the procedure. No significant complications or 30-day mortality was noted.

**CONCLUSIONS:** A new method at lung nodule is described with good preliminary results. The method appears safe and allows long time interval between CT-guided localization and VATS.

**Title:** Vortex Dissaggregation for Flow Cytometry: A Tissue Preserving Method

**Presenter:** CPT Jeffrey A. Vos, MC

**Department:** Department of Pathology

**Mentor:** LTC Mark D. Brissette, MC

**Abstract:**

**Background:** There are many approaches to obtaining single cells from tissue for flow cytometric immunophenotyping; however, all of these methods result in tissue that is too disrupted for subsequent histologic examination. We introduce a new technique for cell dissociation which preserves tissue for histology. This is especially important with small specimens for which this type of correlation is critical.

**Methods:** Fresh tissue to include biopsies from lymph node, GI tract, skin, and a variety of other sites, in addition to cores of inaspirable bone marrows, were briefly vortexed or vigorously shaken until the RPMI cell culture medium became cloudy. Larger specimens were sectioned before disaggregating, while smaller ones were vortexed in toto. Resultant flow cytometric analyses were compared to the histology (prepared from the vortexed tissue) and, in some cases, to the immunohistochemistry (IHC) to determine if the data were concordant.

**Results:** Cell suspensions of 88 specimens-including 40 lymph nodes, 16 bone marrow cores, 10 GI biopsies, 7 skin biopsies, and 15 miscellaneous specimens-were prepared via vortex disaggregation. Flow cytometric analysis of 80 specimens (90.9%) showed adequacy of material and diagnostic correlation with the histology and IHC. Of the 8 cases (9.1%) that were uninterpretable, inadequate, or discordant with the histology and/or IHC, 7 were attributable to significant specimen fibrosis or necrosis. With respect to tissue type, this method produced diagnostic cell suspensions for most lymph nodes (95.0%), GI biopsies (90.0%), and bone marrow cores (87.5%); however, it showed considerable limitation for skin samples.

**Conclusion:** Disaggregation of tissue for flow cytometric analysis by vortexing provides adequate and representative cellular material. This technique is ideal for small biopsies where tissue preservation for histology and special studies is paramount. In addition, specimen preparation by this alternative approach is rapid, technically simple, inexpensive, and permits minimal handling of unfixed tissue.



**Session 4:**  
**Experimental Design**  
**Moderator: MAJ L. Layne Norlund, VC**

The category of "Experimental Design" encompasses the basic science projects. This type of research typically will investigate a fundamental principle of cell biology or physiology, and is the easiest in which to appreciate the values of hypothesis, objective and experimental design. The importance of adherence to these values becomes clear in the ethical imperatives of clinical research. These ethical imperatives involve protection of research subjects, whether animal or human. Above all, rigorous experimental design, facilitates the search for truth, aiding investigators in avoiding fatal flaws. These flaws may remain unrecognized and could lead to false conclusions. We have seen in the papers already presented today that the importance of a hypothesis, objective and good experimental design is consistent throughout any research, including the scientific approach to managed care, military unique research and medical education research.

The range of topics and experimental models that was presented last year was impressive. At least two of the studies have been published, one in Cancer, the other in Urologic Oncology. Many of the others have been presented at national and international meetings, several winning awards.

The papers being presented today are equally impressive. One was truly a collaborative effort, involving sample collection in the Antarctic, three were primarily performed in the DCI laboratories and animal care facility, and two were performed in the patient care arena. All project the creativity present within the people of Madigan.

Some may view basic science research projects as less important or necessary in a setting such as Madigan compared to other types of research. However, another view is that basic science projects and the disciplined approach necessary for their success are a critical step in the training of physicians and nurses who then proceed to complete other projects and become the mentors for the next generation. The principles of study design, execution, and data analysis that are learned in a laboratory or carefully designed project utilizing human or animal subjects are relevant to the success of any research project. As in industry, in medicine the time lag between an idea being in the realm of basic science and practical application is becoming much shorter. I would not be surprised to find that some of the ideas presented in today's Experimental Design section will soon be applied to patient care. In many ways, researchers at Madigan are at the front of the wave that is leading the pathway of change in medicine.

**Title:** The effect of patient positioning during administration of 0.5% isobaric bupivacaine on sensory block level.

**Presenter:** CPT Christopher B. Domer, AN

**Department:** Nurse Anesthesia MS Program

**Mentor:** MAJ Mark Hachey, AN

**Abstract:**

**Introduction:** There have been several studies comparing sensory block level achieved when using bupivacaine solutions of different baricities for spinal anesthesia; however, there is very little research describing the effect of position on sensory block level achieved when using isobaric bupivacaine exclusively. The purpose of this study is to examine the effect of patient position on the subsequent height of sensory block achieved following administration of an isobaric anesthetic solution into the subarachnoid space.

**Methods:** The study will involve 42 patients between the ages of 18 and 65 scheduled for elective lower extremity surgery. The study design is quasi-experimental and prospective. Neither the researcher nor the patient will be blinded to which group the patient is assigned because position during administration will be manipulated. Subjects will be randomly assigned to one of

three groups: Group 1- spinal anesthetic administered with the subject in the lateral decubitus position and then placed supine, Group 2- spinal anesthetic administered with the subject in the seated position and then placed supine, Group 3- spinal anesthetic administered with the subject in the seated position, subject to remain seated for 2.5 minutes before being placed supine. Each subject will receive 3 ml of 0.5% isobaric bupivacaine. The investigator performing the spinal anesthetic will record the sensory level block at 5,10,15, and 30 minutes after injection of the anesthetic solution.

Results: Study currently being conducted. Approval obtained from the Clinical Investigations and Institutional Review Board at Madigan Army Medical Center, Tacoma, Washington and University of Texas Health Science Center, Houston, Texas. Trial data collection, consisting of a pilot study with the first 6 subjects began in January 2000. Projected completion date is May 2000.

**Title:** Bioabsorption Qualities of Chitosan Absorbable Vascular Templates

**Presenter:** CPT Mohamad I. Haque, MC

**Department:** Department of Surgery

**Mentor:** LTC Kenneth Azarow, MC

**Abstract:**

Background: An association via CRADA between the United States Pacific Lab Northwest (Battelle Corp.) and NIAMC was created in 1997. The purpose of this collaboration was to evaluate biodegradable templates in the vascular and tracheobronchial systems. In the vascular model chitosan templates were tested. Polyphosphazene templates are currently being revised for tracheobronchial insertion. The goal of our project is to develop and test chitosan based templates for vascular system. Chitosans, a (1,4)-linked 2-amino-2-deoxy-B-D-glucans are a family of biodegradable and biocompatible cationic polysaccharides. Polyphosphazene is a more rigid substance comprised of repeating aromatic rings without side chains. The scope of endovascular surgical techniques has expanded to include the treatment of diseases considered at one time to be amenable only to surgical treatment. The development of the biodegradable template follows as an extension of current permanent stent technology. Here we describe the in vivo response to placement of chitosan template in a porcine artery. Four attempts at production of a template for tracheal placement yielded models of proper size but of inadequate expandability and rigidity to test in vivo.

Study Design: Ultrapure chitosan (Carbomer, Inc.), heparin sodium salt and lysozyme (Sigma Chemical Company), contrast agents MD-76R and Oxilan 350 were used to give radiopaque quality. Eight, Ten, Twelve French vascular catheters and dilators and balloon angioplasty catheter (Cook), ten balloon expandable stents used for endovascular placement (Palmaz). Prototype chitosan vascular templates were obtained by a dip coating method in which alternate layers of chitosan were coagulated with non-solvents or heparin. Additional heparin was also introduced into a ready template via a solution sorption method. The amount of loaded and released heparin was determined using Azure H colorimetric assay. In vitro enzymatic degradation of templates was evaluated using lysozyme solutions in phosphate buffered saline. Mechanical properties were analyzed using Dynamic Mechanical Analyzer, DMA-7, Perkin Elmer. Microstructure of freeze-dried templates was investigated by field emission scanning electron microscopy (FE SEM) using LEO 982 electron microscope.

In vivo deployment of the templates was undertaken in a surgical suite with fluoroscopic capabilities in ten full-sized pigs (sus scrofa) under general anesthesia and sterile surgical technique. A left groin incision was made and the iliac arteries exposed. Proximal and distal control was established and transverse arteriotomy made after the pigs were systemically heparinized. Multiple arterial dilators were then introduced in an antegrade fashion and deployment location confirmed by arteriography. Using a closed catheter technique the balloon

catheter was advanced under fluoroscopic guidance and the introducer catheter withdrawn to expose the balloon catheter and template. The balloon was then expanded- deploying the Palmaz stent with chitosan template anchored distally. Patency and deployment of the stent- template complex was confirmed by arteriogram. The arteriotomy was then repaired and wounds closed. The pigs were then recovered and sacrificed at 1,2,3 and 4 weeks post-stent placement and arterial sections taken for microscopic analysis.

**Results:** On hematoxylin and eosin staining of the section arterial samples, a marked inflammatory response was noted and progressed with duration of in vivo contact. A giant cell foreign body reaction coupled with intense intimal hyperplasia and organized thrombus was also noted and progressed with duration of time in vivo. Also noted was the degradation of the template material with only small remnant of material noted within the giant cell by week four. Clinically none of the pigs developed limb ischemia or evidence of thrombo-embolic events. There was no evidence of wound infection. No animals were sacrificed prior to the planned interval date.

**Conclusions:** In this preliminary in vivo study, the chitosan template proved to be biodegradable but elicited an intense thrombotic and foreign body reaction despite heparin bonding. Further investigation is ongoing as to decreasing the thrombogenic and antigenic qualities of the template materials by either alteration of the base material or addition of bioactive side chains.

Further work in prototype development with bioengineered tissue mold tracheal stents using polyphosphazene is currently on going.

**Title:** Gastric vs Jejunal Feeding: Nutritional Outcome and Pneumonia

**Presenter:** Mary S. McCarthy, RN, MN

**Department:** Department of Nursing, Nursing Research Service

**Mentor:** LTC Bernard Roth, MC

**Abstract:**

The purpose of this research was to compare nutritional outcomes of patients randomized to gastric or jejunal tube feeding as measured by biochemical parameters, daily caloric intake and indirect calorimetry. This study also compared rates of nosocomial pneumonia between feeding groups.

This randomized, prospective clinical trial used a convenience sample of adult ICU patients in a military medical center from September 1996 through November 1999. Fifty-three patients were consented with feeding initiated in forty-nine: 23 gastric, 26 jejunal, with 7 crossovers to gastric. Nutritional parameters recorded for each group included prescribed energy goal (kcal/day), % goal achieved, albumin and prealbumin values, indirect calorimetry, and nitrogen balance studies. Reports of gastrointestinal complications and aspiration concerns were recorded. Nosocomial pneumonia was evaluated using clinical, radiologic, and microbiologic criteria.

Statistical analysis is currently underway. Repeated measures of analysis of variance (ANOVA) will examine pre-feeding and post-feeding outcomes between the two treatment groups. Chi-square analyses will compare rates of complications for the two groups. Preliminary analysis revealed an average "pre-feeding" prealbumin value of 10.8 g/dl (normal 18-45 g/dl) and the ability for subjects to receive 85% of their goal intake, regardless of feeding group. Noteworthy clinical observations included difficulty with successful feeding tube placement and maintenance of jejunal feeding tubes. Diarrhea was a prevalent gastrointestinal concern, regardless of feeding route.

There is strong evidence that patients presenting to the ICU are undernourished based on height-weight standards and biochemical indices. Indirect calorimetry offered valuable data for critically ill patients with complex metabolic demands. It is incumbent upon health care team members to recommend early nutritional support as multiple studies show that compared to well-

nourished patients, malnourished patients endure slower healing, more complications, increased morbidity and mortality rates, and longer hospital stays. Early multidisciplinary nutritional intervention promotes healing, minimizes complications and enhances rehabilitative success.

**Title:** Continuous Intrathecal Baclofen Infusion in Children with Spasticity of Cerebral Origin

**Presenter:** Lt Col William M. Campbell, MC, USAF

**Department:** Department of Pediatrics, Developmental Pediatrics

**Mentor:** John F. McLaughlin, MD, FAAP, Children's Hospital and Regional Medical Center, Seattle, WA

**Abstract:**

We report the safety and efficacy of continuous intrathecal baclofen infusion (CITB) in children and adolescents with spasticity of cerebral origin.

**Methods:** This was a prospective, observational study at a regional tertiary children's hospital. Subjects were twenty-one consecutive patients with severe spasticity of cerebral origin who underwent CITB pump implantation at a median age of 12 years (range four to 20 years), between 1994 and 1998. Outcome measures included: Spasticity Measurement System (SMS); Ashworth spasticity scale; Gross Motor Function Measure (GMFM); Pediatric Evaluation of Disability Inventory (PEDI); treatment goals and other benefits achieved; adverse events.

**Results:** Fourteen patients completed at least six months of follow-up. SMS scores improved in all six patients tested. Mean Ashworth lower extremity average score decreased 1.3 points. GMFM and PEDI showed no functional change. 94% of treatment goals, including reduction of medications and improvements in comfort, function, and ease of care, were at least partially achieved. During 528 patient-months of pump operation, there were nine device-related adverse events: empty pump (5); catheter breakage (3); pump malfunction (1). There were 10 medical-surgical problems: CSF leak (5); pump site infection with sepsis (1); catheter transection (1); pump misinjection (1); other (2). There were 10 surgical procedures for device-related or medical-surgical problems. Other adverse events included transiently decreased function and/or increased tone, decubiti, and constipation. There were three deaths unrelated to treatment.

**Conclusions:** CITB in children with spasticity of cerebral origin appears to be effective in reducing spasticity and may improve comfort, function, and ease of care. Adverse events are common but are often related to preexisting problems.

**Title:** Fetal Hypoperfusion Causes Increased Interleukin-6 Production in the Isolated Dually Perfused Placental Cotyledon

**Presenter:** CPT Brian Pierce, MC

**Department:** Department of Obstetrics/Gynecology, Maternal Fetal Medicine Fellowship

**Mentor:** LtCol Byron Calhoun, MC USAF

**Abstract:**

**OBJECTIVE:** To determine whether exposure of the isolated perfused human placental cotyledon to different fetal circuit perfusion rates, and concomitant pressure differences, alters placental production of IL-6.

**STUDY DESIGN:** The maternal and fetal circulation of two cotyledons from 5 placentas were perfused for four hours. The fetal circulation of one cotyledon was perfused with HBSS at a low rate of 1 cc/min, the other at high rate of 10 cc/min. The maternal circulation of each cotyledon was perfused at 10 cc/min. Effluents from the fetal circulation were collected at hourly intervals and

IL-6 concentrations were determined by ELISA. IL-6 concentrations with an estimated normal physiologic fetal circulation rate of 4 cc/min were compared with the low and high flow results.

**RESULTS:** Concentrations of IL-6 increased exponentially over time at all perfusion rates, as did the mean difference. Statistically significant differences were achieved at 2, 3, and 4 hours. Mean Perfusion Pressures were also statistically different.

**CONCLUSION:** Decreased fetal circulation flow rates result in an increased production of IL-6. This may implicate fetal placental hypoperfusion in the pathophysiology of cerebral palsy.

**Title:** Gastrin Releasing Peptide: A Potential Growth Factor Expressed in Human Neuroblastoma Tumors

**Presenter:** CPT James A. Sebesta, MC

**Department:** Department of Surgery

**Mentor:** LTC Kenneth S. Azarow, MC

**Abstract:**

**PURPOSE:** Gastrin releasing peptide (GRP) is a 27 amino acid neuropeptide that has been identified in the cytoplasm of many neuroendocrine tumors. GRP has been labeled as an autocrine growth factor in small cell lung carcinomas. Recent work has also shown this to be true in the growth of neuroblastoma Tells in vitro. The purpose of this study was to demonstrate GRP and its receptor (GRP-R) in resected human neuroblastomas and to correlate the presence or absence with other known predictors of poor prognosis.

**METHODS:** To demonstrate the presence of GRP and GRP-R mRNA, total RNA was extracted from human neuroblastoma cells. A reverse transcription polymerase chain reaction was then performed using specific primers. The products of the reverse transcription PCR were then confirmed to be GRP and GRP-R CDNA by southern blot analysis. The reverse transcription PCR products were then sequenced and these sequences were compared to the know sequences of GRP and GRP-R DNA.

**RESULTS:** N = 19. GRP and GRP-R mRNA was present in all neuroblastoma specimens. Although no correlation with other known predictors of poor prognosis existed, transcripts of four different sizes (400, 450, 500, and 950 base pairs) were seen in the GRP transcripts. The sequences of the 950 base pairs sized transcript reverse transcription PCR products were identical to the known GRP.

**CONCLUSION:** We conclude that Gastrin releasing peptide and Gastrin releasing peptide receptor mRNA are present in A human neuroblastomas. The presence of four different transcript sizes, with only the largest one matching with the known Gastrin releasing peptide, suggests alternate splicing (a known feature of growth factors in malignant tumors). Although it appears to lack prognostic significance, its ubiquitous nature in the tumor suggests it may be a useful target to base future treatment modalities.

**Session 5:**  
**Case Report**  
**Moderator: COL Romeo Perez, MC**

Science and medicine depend on communication, especially written communication from one scholar to another, to transmit observations, conclusions, interpretations, and speculations. The peer-review system has developed over the last 300 years as the principal form of this communication. The critical importance of the timely observation, thoughtfully researched, and carefully presented for review by ones peers remains the keystone for most of the advances in clinical investigation and clinical practice. It is through these little discoveries that a specific hypothesis can be formulated and tested in well-designed clinical studies. New diagnostic methods and therapies are validated through clinical trials. The series of presentations in this segment of the program will focus on brief descriptions of cases of a particular condition that are both unusual and provide new insight into diagnosis and or management. A brief review of pertinent literature and appropriate management implications are included.

**Title:** The Use of Polymerized Bovine Hemoglobin in a Patient with Severe, Refractory Immune Pancytopenia

**Presenter:** John Mullon, MD

**Department:** Department of Medicine

**Mentor:** LTC George Giacompe, MC

**Abstract:**

**Background:** Blood substitutes which lack cell surface antigenicity may play a role in the treatment of autoimmune hemolytic anemias refractory to red blood cell transfusions. We report compassionate use of a polymerized form of bovine hemoglobin, BBOC-201 (Hemopure, Biopure Corporation, Cambridge, MA), as a potentially life-saving intervention in a patient with refractory autoimmune pancytopenia.

**Methods:** We continuously monitored hemodynamic response and measures of ischemia throughout the course of therapy. Additional units of HBOC-201 were administered in response to hemodynamic decline, evidence of ischemia, or to maintain a serum hemoglobin level > 4 grams per decaliter (2.47 mmol/Lit).

**Results:** Eleven units of BBOC-201 were administered over a seven-day period. On HBOC-201 therapy the patient tolerated a hematocrit as low as 4.4 percent without end-organ ischemia. Before HBOC-201 therapy the patient manifested angina and ischemic electrocardiogram changes at a hematocrit of 7.5 percent. The cumulative dose of 4.9 grams per kilogram is the largest quantity of this product reportedly administered to a human subject. In spite of this no side effects directly attributable to BBOC-201 were appreciated. The patient was discharged to home with on hospital day 152. Subsequent follow-up revealed no long-term sequelae.

**Conclusions:** We report the first use of a blood substitute as a potentially life-saving intervention in a patient with refractory hemolytic anemia. We additionally report the largest dose of HBOC-201 administered to a human subject, without significant side effects noted. Blood substitutes may play a valuable adjunct role in the treatment of refractory hemolytic anemias.

**Title:** Metabolic Myopathy in an Active Duty Soldier

**Presenter:** CPT Anne B. Rossignol, MC

**Department:** Department of Medicine, Internal Medicine Service

**Mentor:** Laura S. Martin, MD, FAAP, FACMG

## **Abstract:**

**Introduction:** Military life often includes unusual stressors such as extremes of physical exertion, sleep deprivation and periods of fasting which may unmask disorders in soldiers which would otherwise remain unrecognized. Extremes of exertion and fasting as seen in basic training can precipitate myoglobinuria. The metabolic myopathies represent a category of inherited disorders which may manifest as exercise intolerance and myoglobinuria. Long term sequelae may include compromised renal function.

**Case Report:** A 26 year old active duty soldier in the US Army was referred to Genetics clinic for evaluation of his myoglobinuria as part of the Medical Evaluation Board process. The patient was in his usual state of good health until approximately three years ago when he experienced excruciating pain over his arms and chest while performing repetitive upper body exercise consisting of lifting his Army duffel bag over his head and multiple sets of push-ups and sit-ups. Subsequent evaluation revealed myoglobinuria and elevated CPK to ~23,000U/L. He was discharged without further assessment and remained symptom free despite a personal exercise program. A similar second episode three years later was precipitated by unit PT. A muscle biopsy was preformed. Histology and immunohistochemistry were normal including the presence of Myophosphorylase and phosphofructokinase activity. No mitochondrial abnormalities were observed. Glycogen and lipid storage were normal. Further biochemical evaluation of the fatty acid metabolic pathway yielded a significant partial deficiency, 35.2 nmol/min/g muscle (reference range 77.8 +/- 13.3 nmol/min/g muscle) of Carnitine Palmitoyl-transferase (CPT) with normal Phosphorylase and Citrate Synthase activity. These results document that the patient is likely to be a manifesting heterozygote of CPT, an autosomal recessive inborn error of metabolism.

**Discussion:** The awareness of the differential diagnoses of myoglobinuria is critical for optimal medical evaluation. A comprehensive approach results in a specific diagnosis providing the basis for appropriate modification of life choices for the patient, his family and the US Army. Our case is a fascinating example of a patient with a previously unrecognized inborn error of fatty acid metabolism which first became evident during Army Basic Training.

**Title:** Vaginal Examination in the Pediatric Patient: The Use of Micro-Hydrovaginostomy

**Presenter:** CPT Jason Parker, MC

**Department:** Department of Obstetrics/Gynecology

**Mentor:** COL Milo L. Hibbert, MC

## **Abstract:**

**Background:** The gynecologic evaluation of pediatric patients is challenging. Special examination techniques are required. We describe the innovative technique of micro-hydrovaginostomy and present 3 cases in which it was employed to facilitate evaluation and treatment.

**Case 1:** A 10 year-old was seen for suspected imperforate hymen. Examination under anesthesia revealed a cribriform hymen with several small openings. Hydrovaginostomy, using a 2-mm endoscope placed through one of the hymeneal perforations, confirmed the diagnosis. The hymeneal bands were incised. **Case 2:** A 4 year-old was seen on two occasions for the complaint of discharge. Not responding to medical management, she underwent hydrovaginostomy using a 4-mm flexible hysteroscope. Under direct endoscopic vision, using a co-axial polyp forceps, an orange crayon was removed. **Case 3:** A 3 year-old was seen for evaluation of vulvar irritation and discharge. Difficult physical examination revealed normal external genitalia, but no obvious vaginal opening. Ultrasound failed to reveal uterine tissue, but ovaries were present. Hydrovaginostomy was performed to assess the degree of "urogenital" vagina, and to rule out the presence of a foreign body or partial imperforate hymen. She was found to have a normal vaginal opening without obstructing hymen and a blind vaginal pouch.



**Conclusion:** Hydrovaginotomy using small diameter endoscopes is a simple, minimally invasive, and effective method of vaginal examination in the pediatric patient. It permits precise and complete diagnosis, directs and assists treatment, and has potential for well-tolerated office use in cooperative patients.

**Title:** Endoscopic resection of nasal septal chondrosarcoma: a report of two cases

**Presenter:** MAJ George L. Coppit, MC

**Department:** Department of Surgery, Otolaryngology Service

**Mentor:** COL Vincent D. Eusterman, MC

**Abstract:**

**Objective:** To introduce a new surgical approach to nasal septal chondrosarcoma that reduces operative time, patient morbidity, and hospital stay.

**Design:** Report of two cases

**Description:** Chondrosarcomas account for 10-20% of malignant primary bone tumors, with only 10% being found in the head and neck. Of these lesions, less than 5% arise from the nasal septum, with only 42 cases reported in the literature. Surgical resection is the treatment of choice. The tumor is generally approached through a LeFort I downfracture or lateral rhinotomy, and can be combined with a bifrontal craniotomy for extensive disease. These procedures have a significant associated morbidity, and can be disfiguring. With the advent of endoscopic surgery, procedures that once required wide exposure with significant morbidity can now be approached with minimal disruption of surrounding normal tissues. We present two cases of extensive nasal septal chondrosarcoma successfully managed via an endoscopic approach. We will compare the endoscopic technique to the standard approach, as well as review each case and provide the most recent follow-up of the patients. Additionally, we will review the epidemiology and pathologic findings in this disease.

**Conclusions:** Endoscopic resection of nasal septal chondrosarcoma is a viable approach when these tumors present without intracranial extension. Total extirpation of the tumor is possible, while reducing surgical time and morbidity to the patient. We have had no evidence of recurrence with our patients with three years of follow-up.



### **Steger Award**

This award is given to a resident, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2000:

*The Effects of Mitomycin-C and Stenting on Airway Wound Healing after Laryngotracheal Reconstruction in a Pig Model* by CPT George L. Coppitt, MC, Otolaryngology Service, Department of Surgery

Other nominees were:

*Vaccinating US Army Soldiers against Lyme Disease: A Cost-effectiveness Analysis* by Arthur B. Cajigal, DO, MPH, Preventive Medicine, Public Health Residency

*Tracheal Mucosal Healing following Moderate Injury Induced by Expandable Metallic Stents* by LCDR Keith M. Ulnick, MC, Otolaryngology Service, Department of Surgery

*Postoperative Management of the Obstructive Sleep Apnea Patient* by LCDR Keith M. Ulnick, MC, Otolaryngology Service, Department of Surgery

### **Fellow's Research Award**

This award is given to a fellow, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2000:

*Hypoperfusion Causes Increased Interleukin-6 and Tumor Necrosis Factor-Alpha Production in the Isolated Dually Perfused Placental Cotyledon* by CPT Brain T. Pierce, MC, Maternal-Fetal Medicine, Department of Obstetrics/Gynecology

Other nominees were:

None.

## Kenyon Joyce Award

This award is given to staff, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2000:

*The Relationship Between Ventilator Inspired Gas Temperature and Tracheal Injury in Neonates*  
by Lori A. Loan, Ph.D., Nursing Research Service

Other nominees were:

*Evidence-based Nursing Interventions to Improve ARDS Patient Outcomes* by LTC Laura R. Brosch, AN, Chief, Surgical Nursing

*Indirect Calorimetry as a Tool to Optimize Disease Management and Patient Outcomes* by Mary S. McCarthy, MN, RN, Nursing Research Service

*Radiation Injuries from Military and Accidental Explosions: A Brief Historical Review* by LTC Wynona M. Bice-Stephens, NC

*Female Airman Readiness: A Leader's Guide* by LTC Byron C. Calhoun, MC and Airman Hartley, Maternal-Fetal Medicine, Department of Obstetrics/Gynecology

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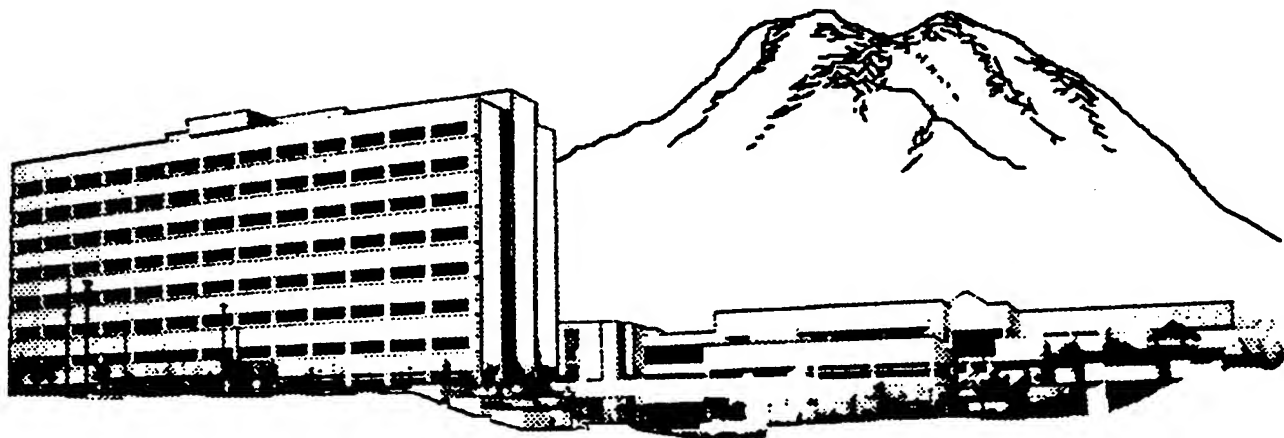
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## Detail Summary Sheets

Department of Anesthesia and Operative Services

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/046

**Status:** Ongoing

**Title:** An Open-label, Long-term Safety and Tolerability Study of Ziconitide Administered Intrathecally to Patients with Chronic, Severe Pain

**Principal Investigator:** MAJ Andrew G Kowal, MC

**Department:** Anesthesia & Operative Services

**Facility:** MAMC

**Associate Investigator(s):** MAJ Stephen L. Bolt, MC

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Jan 10

**Periodic Review:**  
N/A

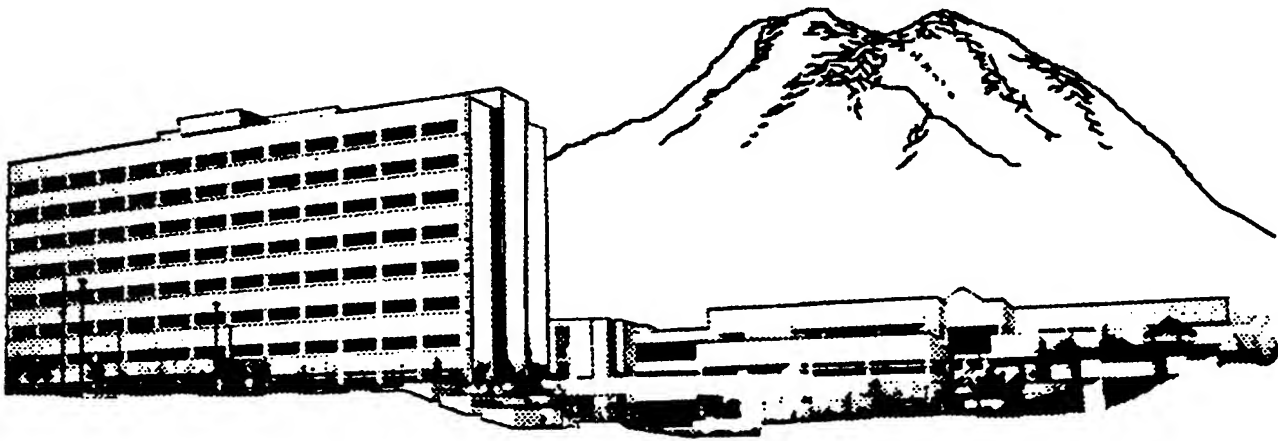
**Study Objective:** The purpose of this study is to assess the long-term safety and tolerability of Ziconitide administered intrathecally to patients with chronic, severe pain.

**Technical Approach:** This is a Phase IIIB, long term, open-label, multicenter study to assess the safety and tolerability of intrathecally administered Ziconitide in up to 700 patients with chronic severe pain. The target population is made up of patients who suffer from chronic, severe pain with intrathecal catheters already in place, or for those whose next line of therapy would require placement of such devices.

Patients will be seen on an outpatient basis. For the first month, they will come in at least twice a week to have a physical assessment and get their dose adjusted accordingly. After the first month, safety assessments and pump refills will be done monthly on an outpatient basis. Demographics and baseline information will be summarized with descriptive statistics. Descriptive statistics will be used to summarize the changes from baseline to the follow-up scheduled time points for the vital sign measurements, ECG results, the Wechsler Memory Scale subtest, Trail Making, parts A and B, and Function Level Assessment. The study will continue until the drug is FDA approved.

**Progress:** No patients have been enrolled in this study in FY00 at MAMC. Patient screening has started.





## Detail Summary Sheets

Admin. Residents  
Deputy Commander for Administration

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/030

**Status:** Completed

**Title:** The Alaska Federal Health Care Partnership: An Approach to Improving the U.S. Coast Guard Health Care System Through Interagency Support

**Principal Investigator:** LT Mark L. Everett, USCG, CAAMA

**Department:** DCA/Admin Residents

**Facility:** MAMC

**Associate Investigator(s):** COL Van R. Booth, MS

**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Jun 00

**Periodic Review:**  
N/A

**Study Objective:** To determine by cost-benefit analysis the optimal approach to joint partnership between DoD Military Health System, VA Health Care System, and USCG in providing health care in Alaska.

**Technical Approach:** MAMC/WRMC will serve as the core facility for the development of this Policy Cost Benefit Analysis. The methodologies used in the current study would parallel that policy research approach with the augmentation of the existence of several years' data within our region with different approaches by sister services. This existing data can be analyzed using microeconomics to evaluate the cost consequence of the variance between pathways.

**Progress:** There are three types of AFHCP initiatives: joint contracting, revenue recapture, and use of technology. This retrospective, descriptive business case study used a cost benefit analysis method called the "balance-sheet" approach to tabulate who bore the costs and who reaped the benefits from these AFHCP initiatives at Alaskan USCG clinics in Fiscal Years 1997 through 1999. The balance-sheet approach facilitated evaluation of quantifiable and unquantifiable changes in cost, quality, and access factors as a basis for program evaluation. The AFHCP initiatives found most beneficial to Alaskan USCG clinics and their constituencies were joint contracting for health care services and in-clinic visiting specialist programs (revenue recapturing). Though only begun in Fiscal Year 1999, the use of teleradiology technology will likely prove beneficial as well. **Conclusions:** The USCG Health Services Program has no formal strategic plan. Its business strategy has been, by default, overwhelmingly opportunistic and reactive in nature. To the extent that approach will remain the business strategy, the USCG should continue to aggressively pursue interagency relationships that support any and all USCG clinics and beneficiaries. Areas for primary focus should be remote clinics responsible for beneficiaries assigned to locales where TPR has been implemented.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/027      **Status:** Completed

**Title:** A Critical Review of the Army Medical Board System - Army-Baylor Graduate Program in Health Care Administration: Graduate Management Project

**Principal Investigator:** CPT Clinton W. Schreckhise, MS

**Department:** DCA/Admin Residents

**Facility:** MAMC

**Associate Investigator(s):** COL Van R. Booth, MS

**Start Date:**  
1/25/2000

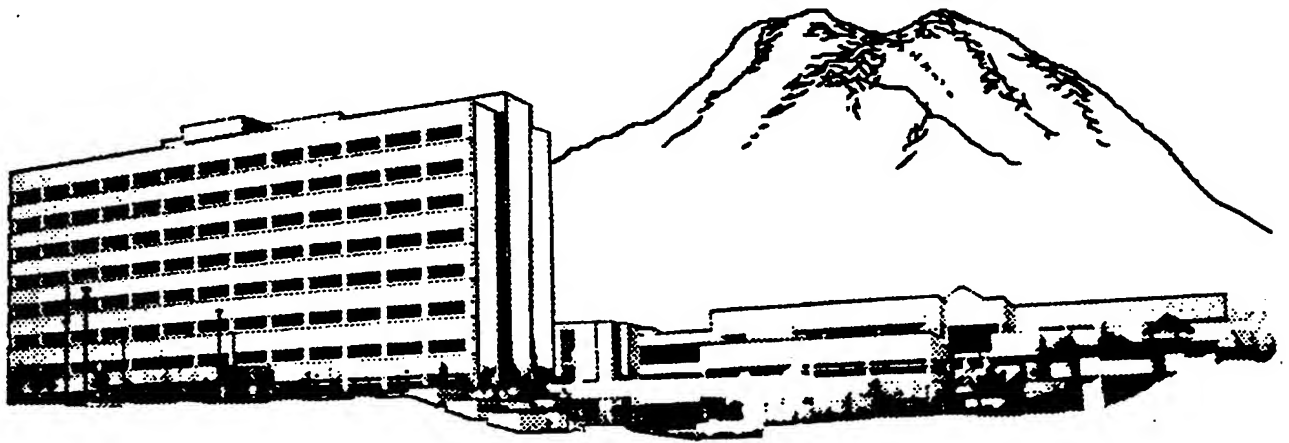
**Est. Completion Date:**  
Mar 00

**Periodic Review:**  
N/A

**Study Objective:** The Department of Defense Military Health System must process the potential loss of service members due to medical illness or injury. The Medical Board System provides the procedural bases for the analyses and fair disposition for service members who can no longer perform their duties. What is the optimal approach and what are the cultural barriers?

**Technical Approach:** The researcher will use a stepwise linear regression to determine relationships among variables in the overall process. By doing a statistical analysis, the researcher will be able to identify where the greatest impediments lie for processing cases. These results will also be compared to the other branches of the military.

**Progress:** Retrospective data, consisting of 200 Medical Evaluation Board cases, were reviewed. The average Medical Evaluation Board processing time at MAMC was 157 days. This time spans from notification of intent to start of MEB to completion. It was found that delivery of care and preparation of the MEB Narrative Summary take up 92.5% of the time. By comparison, two sister services accomplish the same MEB tasks much quicker, with the Air Force completing MEBs within 21 days on average. **Conclusions:** Consider the Air Force approach and adopting processes as practicable considering mission requirements. Also, findings indicate an error in how the Army counts processing days based on the automated tracking tool used. Modifications to the software, or by-hand calculations, are necessary to accurately report processing times. Finally, the Army should reconsider addressing all of a soldier's medical complaints rather than simply focusing on conditions considered disqualifying for service.



## **Detail Summary Sheets**

Department of Clinical Investigation

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/104	<b>Status:</b> Terminated
<b>Title:</b> Expression of Angiostatin and TSP1 in Human Microvascular Endothelial Cells and Breast Cancer Cells: In Vitro Study of a Potentially Superior Antiangiogenic Activity		
<b>Principal Investigator:</b> Jeff M. Bullock, M.S.		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Katherine H. Moore, Ph.D.; CPT Aziz N. Qabar, MS; James R. Wright, M.T.		
<b>Start Date:</b> 9/15/1998	<b>Est. Completion Date:</b> Aug 99	<b>Periodic Review:</b> 7/27/2000

**Study Objective:** (1) To establish the profile of Plasminogen and TSP1 expression in quiescent and proliferating human microvascular endothelial cells and two breast cancer cell lines, MCF-7 and MDA-431 and (2) to compare the antiangiogenic phenotype of Angiostatin, TSP1, and type I repeat truncations on the proliferation of human microvascular endothelial cells (HMVEC) in vitro.

**Technical Approach:** This study is designed to examine the possibility of a combinatorial antiangiogenic activity in vitro, where the effectiveness of two or more antiangiogenic molecules against proliferating human microvascular endothelial cells (HMVEC) is evaluated. The expression of an angiostatin, a proteolytic fragment of Plasminogen, in the non-invasive breast cancer cell lines MCF-7, the invasive breast cancer cells line MDA-431, and HMVEC is evaluated using Western blots, Northern blots, and polymerase chain reaction (PCR). A profile of TSP1 and angiostatin expression in these cells will be established, as a function of time in culture and following bFGF-induced proliferation. Moreover, the inhibitory effect of truncated forms of TSP1 on HMVEC angiogenesis will be determined and compared to that of both TSP1 and angiostatin separately. Finally, a combination of two or more of the antiangiogenic molecules will be tested to determine the most potent inhibitory activity.

**Progress:** This protocol has been reported as terminated, 14 Aug 00, due to the PCS of its original principal investigator and change of duties and time commitments of the associate investigator.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/023

**Status:** Ongoing

**Title:** Cholesterol Transfer in the Term Human Placenta: The Effects of Lipoprotein Cholesterol Infusion in the Dual Perfused Isolated Human Placental Cotyledon Model

**Principal Investigator:** COL Roderick F. Hume, MC

**Department:** Clinical Investigation

**Facility:** MAMC

**Associate Investigator(s):** Laura S. Martin, M.D.; MAJ Elizabeth G. Hancock, MC ; CPT Todd M. Rossignol, MS ; LTC Jerome B. Myers, MC; CPT David J. Phillips, MS; MAJ Bardett Fawcette, MC USAF; Robert Steiner, MD; William E. Connor, MD

**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Nov 00

**Periodic Review:**  
N/A

**Study Objective:** To identify and quantitate the pharmacokinetics of cholesterol transfer in the term human placenta by investigating the effect of lipoprotein cholesterol infusion on the maternal-fetal transfer of cholesterol across the placenta using the dually perfused isolated human cotyledon.

**Technical Approach:** The placentas will be collected immediately after deliver and transported to the perfusion laboratory. After visual inspection for lacerations or infarcts, the fetal surface will be inspected for a chorionic artery and vein pair supplying a cotyledon. The chorionic artery and vein of the selected cotyledon will be cannulated. This section of the placenta will be clamped into a holder and then the cotyledon will be transferred to a temperature-controlled chamber maintained at 37 degrees C. A second cotyledon will be prepared in an identical manner by a second investigator. All perfusions will be started within 20 minutes of placenta delivery. After establishing baseline perfusion steady states for approximately 30 minutes using Hanks' balanced salt solutions, perfusion pressures and effluents will be obtained. At this time a solution of Hanks' balanced solution with albumin and heparin with various concentrations of cholesterol (100-400 mol/L) will be switched with the perfusate of one of the cotyledons. After a 20 minute steady state period perfusion pressures and perfusates will be collected, goal out of 4-6 hours. Perfusate cholesterol concentrations relevant to natural occurring maternal-placental cholesterol concentrations will be obtained. There will be a total of 4 collection periods. Remaining placental tissue not used in the experiment may be submitted to pathology for evaluation to assure normal placental histology or frozen for further study.

**Progress:** This bench study has not yet begun at MAMC.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 97/128	Status: Completed
Title: Enhancing the Effectiveness of Tamoxifen Therapy in Breast Cancer		
Principal Investigator: COL Roderick F. Hume, MC		
Department: Clinical Investigation	Facility: MAMC	
Associate Investigator(s): MAJ Richard F. Williams, MC; Maryls J.M. Nessel, Ph.D.; Katherine H. Moore, Ph.D.; CPT Todd M. Rossignol, MS		
Start Date: 8/15/1997	Est. Completion Date: Oct 00	Periodic Review: 7/25/2000

**Study Objective:** (1) Investigate the mechanism by which SHBG and tamoxifen mediate a reduction in cell number in MCF-7 breast cancer cells in-vitro by measuring their effect on both G1 cell cycle arrest and apoptosis, as well as level of expression of factors which mediate apoptosis such as Bcl-2 and Bax; (2) study the regulation of production of endogenous SHBG by estrogen and tamoxifen, as well as agents reported to affect SHBG levels on other systems, such as insulin, prolactin, androgen, and cAMP; and (3) determine the effect of simultaneous treatment of MCF-7 cells with exogenous SHBG and tamoxifen on cell growth and apoptosis.

**Technical Approach:** We will be exploring the novel idea that interaction occurs between two effectors of steroid response in breast cancer cells, tamoxifen and sex hormone binding globulin (SHBG), resulting in a reduction of the rate of cell growth and increasing the rate of cell death. This study may provide the foundation to developing more effective treatment of breast cancer. The inhibitory effect of tamoxifen, a partial antagonist of estrogen action, on cell growth has been well documented. Evidence for an effect of tamoxifen on programmed cell death (apoptosis) has been reported recently. In preliminary studies in our laboratory, tamoxifen decreases the level of the anti-apoptosis factor Bcl-2, and this effect appears to depend on the level of estrogen to which cells are exposed prior to treatment. An inhibitory effect of cAMP on cell growth in response to estrogen has been recently shown by others and confirmed in our laboratory. Additionally, treatment with exogenous SHBG has been shown to increase cAMP levels and inhibit response to estrogen. Our group has demonstrated that SHBG is produced endogenously by MCF-7 breast cancer cells. Interestingly, recent data suggest that serum SHBG levels increase in patients treated with estrogen antagonists, suggesting that antiestrogen agents may regulate SHBG production. A potentially important aspect of this study would be the discovery of a means to increase the inhibitory effect of antiestrogens on breast cancer cell growth and/or cell death by modulation of SHBG levels as addressed in objective 2. If one of these agents is found to modulate SHBG levels, and if SHBG is shown to modulate the inhibitory effect of tamoxifen, a potential means of biologically increasing the effectiveness of breast cancer treatment with antiestrogens could be identified.

**Progress:** Conclusions: Tamoxifen strongly affected both cell count and telomerase activity within the 10-8M concentration of both cell lines. Cells were able to overcome drug inhibition at all other doses after 4 days. Telomerase activity and cell proliferation were correlated in both cell lines and depended on drug concentration. Tamoxifen showed long term effects on cell proliferation of the MCF-7 cells.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/073		<b>Status:</b> Ongoing	
<b>Title:</b> Comparative Medical/Surgical Research and Development (Limited)					
<b>Principal Investigator:</b> MAJ L. Layne Norlund, VC					
<b>Department:</b> Clinical Investigation				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.					
<b>Start Date:</b> 3/8/2000		<b>Est. Completion Date:</b> Mar 03		<b>Periodic Review:</b> N/A	

**Study Objective:** (1) To facilitate preliminary investigations of proposed animal research models and pilot studies, as well as the practice of newly described surgical procedures on animals prior to use in human patients; in an effort to refine and reduce the sacrifice of animals and enhance the quality and effectiveness of medical/surgical patient services at MAMC and (2) To provide uniform standards and assurances of proper animal care and use in the conduct of limited animal model development, pilot studies, and surgical advancement training proposed by MAMC-affiliated medical staff.

**Technical Approach:** This protocol is designed to facilitate preliminary investigative medical and surgical research and development as described below: a) development or refinement of animal models for medical/surgical research or training; b) limited pilot studies (animal) that are preliminary to more extensive research proposals; c) practice of newly described surgical procedures, in animal models, prior to utilization in the MAMC human surgical patient population. Animal use in these investigative pursuits will generally be limited to not more than four (4) animals per co-investigator or procedure, and will be conducted as acute (non-survival) experiments unless animal survival is specifically justified. Details of proposed model development or refinement, pilot studies, or surgical procedure practice will be provided as procedure specific addenda to this standing protocol. This protocol will only be used for preliminary pilot/model development and MAMC surgical care advancement, and will not be used to generate data sufficient for publication in scientific journals.

**Progress:** On 5 Sep 00, 2 pigs were used for training 4 Cardiovascular surgeons, 1 Perfusionist, 2 OR Nurses, and 4 OR technicians in the intraoperative use of a biventricular cardiac assist device (BVAD), manufactured by ABIOMED, Inc. An in-vivo animal surgical lab is required by FDA/Manufacturer agreement before surgeons are certified to use the ABIOMED BVAD in human patients. This training lab was highly successful in acquainting surgeons and OR support personnel in the use of this device.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/146	<b>Status:</b> Ongoing
<b>Title:</b> Biomedical Research or Training Using Animal Tissues Only		
<b>Principal Investigator:</b> MAJ L. Layne Norlund, VC		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start Date:</b> 9/13/2000	<b>Est. Completion Date:</b> Sep 03	<b>Periodic Review:</b> N/A

**Study Objective:** To reduce live animal use in biomedical research or training at MAMC, by facilitating animal tissue use as alternative research/training models, where feasible.

**Technical Approach:** Animal cadavers or tissues used under this protocol will be derived from MAMC IACUC-approved animal use protocols, other AAALAC accredited research institutions, or from local commercial slaughter houses unless otherwise specified in addenda and approved by the IACUC in advance of procurement. This document will serve as a generic, IACUC-approved protocol providing specifications and assurances for animal tissue use in biomedical research or training, which will be adhered to by all persons using this protocol. Specific activities differing from the generic provisions of this protocol will require description and/or justification by addendum, and IACUC approval, prior to conducting the described research or training.

**Progress:** This protocol was recently approved by the IACUC and has not yet been initiated at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/043	<b>Status:</b> Ongoing
<b>Title:</b> Immunohistochemical and Molecular Biotechnologic Detection of the Human Adrenomedullin Receptor		
<b>Principal Investigator:</b> CPT Todd M. Rossignol, MS		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT David J. Phillips, MS; MAJ Christina Apodaca, MC; LTC Byron C. Calhoun, MC, USAF; COL Roderick F. Hume, MC		
<b>Start Date:</b> 2/22/2000	<b>Est. Completion Date:</b> Sep 00	<b>Periodic Review:</b> N/A

**Study Objective:** (1) Produce a polyclonal antibody that recognizes both the native and denatured forms of the human adrenomedullin receptor. This will allow the detection of this receptor in both immunohistochemical assays and western blot analysis. (2) Perform immunohistochemical assays and western blot analysis on various compartments of the human placenta.

**Technical Approach:** A peptide sequence corresponding to amino acids 5-19 and 244-254 of the human adrenomedullin receptor will be sent to Sigma Genosys to be synthesized and conjugated to KLH. This peptide will then be used to produce polyclonal antibodies. Once the antibodies are produced, preliminary immunohistochemical assays will be run to determine the proper dilution of the antibody. In order to verify that the antibody is recognizing the intended protein, the antibody is pre-incubated with the purified antigen. Upon identifying eligible placentas, the primary investigator will be notified at the time of the delivery. The placenta will be obtained immediately after delivery and placed on ice. Approximately 5 grams each of the placental amnion, cotyledon, umbilical vein and umbilical artery will be dissected and isolated. 1-2 cm<sup>2</sup> area of the frozen tissue sections will be mounted on the cryostat using OCT. The tissues will be sliced into 5-10 uM sections. These sections will be probed with the primary antibody (Rabbit Anti-Adrenomedullin Receptor IgG) after being blocked and then after washing they will be probed with the secondary antibody (Mouse Antirabbit IgG) conjugated with Fluorescein Isothiocyanate (FITC). The slides will be viewed using a fluorescent microscope with an excitation wavelength of 450-490 nm and filtered at 520-560 nm.

**Progress:** This recently approved protocol has not initiated data collection as of the time of this report. Preliminary lab setup and biotechnologic methodologies are in place to begin data collection in the near future.

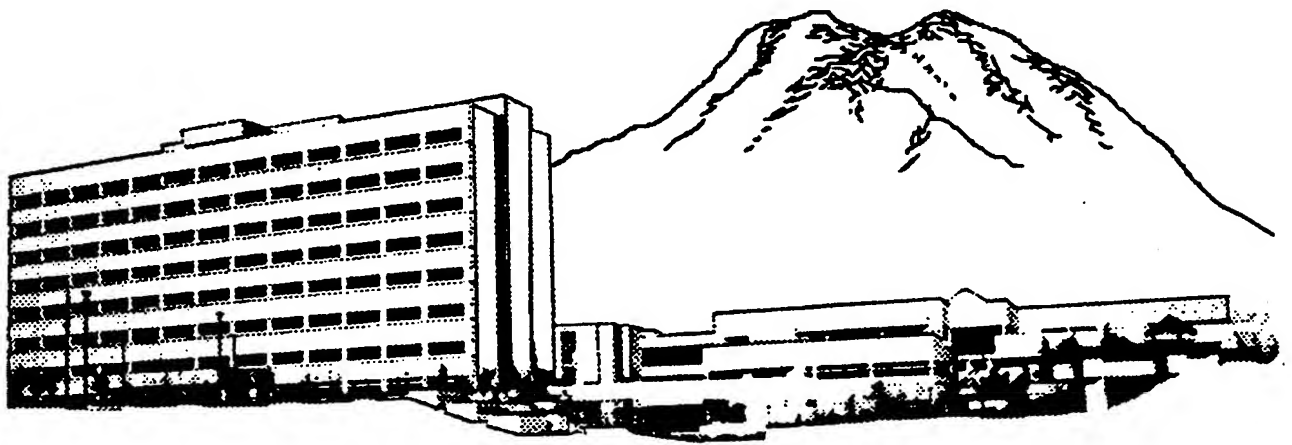
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/025	<b>Status:</b> Ongoing
<b>Title:</b> The Department of Clinical Investigation's Molecular Biology Short Course for Physicians		
<b>Principal Investigator:</b> CPT Todd M. Rossignol, MS		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Rodger K. Martin, MS; CPT Wade K. Aldous, MS; CPT Aziz N. Qabar, MS		
<b>Start Date:</b> 1/20/1995	<b>Est. Completion Date:</b> Jun 96	<b>Periodic Review:</b> 2/22/2000

**Study Objective:** To familiarize MAMC residents, fellows, and staff physicians with the research capabilities and resources of the Department of Clinical Investigation. To support MAMC Graduate Medical Education through instruction and research. To foster an appreciation of molecular biology concepts in residents, fellows, and staff physicians and to augment their understanding of the scientific literature. To encourage residents, fellows and staff physicians to develop research protocols incorporating these technologies.

**Technical Approach:** This course is designed to familiarize physicians with the most commonly encountered molecular approaches in the scientific and clinical literature. It is hoped that this will foster more critical reading of the literature as well as encouraging the development of research protocols employing these technologies. Although six weeks in duration, students will be required to attend two hours of lecture per week in addition to approximately seven hours of laboratory exercises. Topics addressed and used in the course range from DNA isolation to cloning and sequencing of PCR products.

**Progress:** No courses were taught in FY00.



## Detail Summary Sheets

### Hospital Dental Clinic

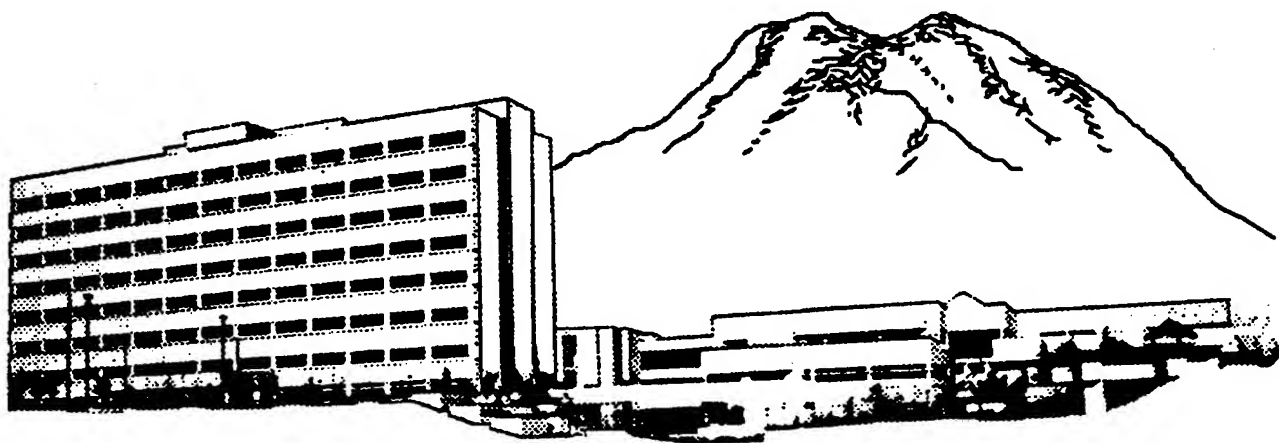
### Detail Summary Sheet

Date: 29 Sep 00	Number: 200/035	Status: Ongoing
Title: Low Energy Laser (helium-neon) Biostimulation and mucosal Wound Healing		
Principal Investigator: MAJ Charles E. Middleton, DC		
Department: Dentistry	Facility: MAMC	
Associate Investigator(s): COL Wayne Olsen, DC; LTC Charles R. Weber, DC; LTC Peter Zagursky, DC		
Start Date: 1/25/2000	Est. Completion Date: Apr 00	Periodic Review: N/A

**Study Objective:** To illustrate that the application of low energy laser radiation to mucosal wounds in vivo results in a shortened healing time and that the hand held laser is an effective device to deliver low-energy radiation.

**Technical Approach:** Fifty patients scheduled for the bilateral surgical extraction of maxillary third molar teeth will have one of two standard vertical releasing incisions lased with a helium-neon hand held laser at time of surgery. The contra-lateral incision will serve as control. The helium-neon laser is a commercially available (laser-pointer) instrument that is highly portable and field ready. This study will attempt to prove that the application of low energy laser radiation to surgical wounds results in a biostimulatory process with resultant shortened healing times. Wound Analysis Index will be secured at 4, 7, 14 and 21 days post-surgery. Lasing energy fluence will be at 1.2 j/cm<sup>2</sup>. The data will then be analyzed for statistical significance.

**Progress:** Thirty-three (33) patients requiring the surgical extraction of maxillary right and left impacted third molar teeth had 1 of 2 full-thickness mucogingival flap incisions lased by a handheld He-Ne diode laser. Fifty-seven percent (57%) of the participant's lased incisions had accelerated healing at post-exposure day 4. Accelerated healing peaked at post-exposure day 8 at sixty-eight percent (68%). There was no difference beyond day 14. This study's results tend to support the biostimulatory properties of low-energy laser irradiation as applied to surgical wounds.



## **Detail Summary Sheets**

Department of Emergency Medicine

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/070	<b>Status:</b> Ongoing
<b>Title:</b> A Survey to Determine the Incidence of Infection in Plantar Puncture Wounds		
<b>Principal Investigator:</b> CPT Charles P. Buck, MC		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Austin W. Burgess, MC; MAJ David A. Della-Giustina, MC		
<b>Start Date:</b> 6/22/1999	<b>Est. Completion Date:</b> Jul 99	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** To determine the incidence of infection in plantar puncture wounds, and to determine if infection rates are different for healthy vs. immune compromised and aggressive vs. conservative initial management groups.

**Technical Approach:** All adult ambulatory patients identified by the triage nurse as having a prior plantar puncture wound will be asked to complete an anonymous survey. Investigators will periodically collect the forms and transfer the data to spreadsheets for further analysis. Method of data analysis: Primary is the overall incidence of infection of plantar puncture wounds, with data analyzed at 95% confidence intervals. Secondary is the infection rate for two groups, which will consist of subjects that had aggressive initial treatment vs. conservative treatment, and those who were healthy at the time of injury vs. those with vascular or immuno-compromising diseases. These groups will be analyzed by Chi-Square to determine statistical significance at  $p < 0.05$ .

**Progress:** Approximately 150 surveys have been returned during FY00, for a total of 200 surveys overall. Surveying continues in order to obtain sufficient data for statistical analysis.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 200/014

Status: Completed

Title: The Incidence of Corneal Freezing Injuries in Military Free Fall Parachutists

Principal Investigator: CPT Leonard Q. Gruppo, Jr., SP

Department: Emergency Medicine

Facility: MAMC

Associate Investigator(s): MAJ Ian S. Wedmore, MC

Start Date:  
11/19/1999

Est. Completion Date:  
Jun 00

Periodic Review:  
N/A

**Study Objective:** Analyze reports of mechanism of injury and symptoms consistent with corneal freezing injury to estimate the incidence and severity of that injury in military free-fall parachutists. If the incidence is significant, recommendations for more definitive studies, medical education for Special Operations Forces (SOF), medics and medical officers, and changes in wind goggle design will be suggested.

**Technical Approach:** In this study, a cover letter, questionnaire, and stamped envelope will be mailed to all team leaders of U.S. Army Special Operations Forces active and reserve HALO teams. Returned data will be statistically analyzed in accordance with the following criteria: (1) Incidence of goggle loss or malalignment, (2) Of those who lost goggles, the incidence of symptoms consistent with c/w corneal freezing, (3) Of those with appropriate symptoms: (A) How many sought medical care, (B) How many required treatment, (C) What was the diagnosis, (D) How long did the symptoms persist, and (E) How many had permanent damage that may be attributable to the injury.

**Progress:** 394 surveys were submitted in this survey. Findings are as follows: Experience of less than 75 jumps is associated with a several fold increase in the incidence of ocular problems. Freezing temperatures produce a several fold increase in the incidence of ocular problems and the frequency those problems affect the ground mission. Data suggests that PRK had no detrimental effect on MFF operations. It may be advantageous to correct vision with PRK rather than wear contact lenses during free fall. Contact lenses were shown to provide no significant protection against adverse ocular symptoms in freezing temperatures, as they tend to dislodge when goggles blow off, causing their use to be associated with a higher incidence of adverse effects on the ground mission than seen overall.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/104

**Status:** Ongoing

**Title:** A Randomized, Placebo-Controlled, Study of Intravenous Magnesium in Acute Benign Headaches

**Principal Investigator:** CPT Kurtis R. Holt, MC

**Department:** Emergency Medicine

**Facility:** MAMC

**Associate Investigator(s):** Marvin K. Valrey, MD; Leonard Frank, MD; Laura Fife, MD; CPT Thomas R. Coomes, MC

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
10/24/2000

**Study Objective:** Our purpose is to evaluate the efficacy of IV magnesium in acute headache pain, in a prospective randomized, double blind, placebo-controlled trial. Because of the difficulty of classification, as well as the desire to make this study more applicable to the typical clinical practice of emergency medicine, we will evaluate all patients who present with benign headache pain.

**Technical Approach:** The Pharmacy will pre-prepare bags of drug and placebo in lots of ten by standard randomization procedures. Each bag will be labeled with a study number, the name of the study, and the date of preparation/expiration. Emergency Department personnel and patients will be blinded to the study treatment. The Pharmacy will hold the randomization code which will only be broken in the event of an emergency. Staff and resident physicians in the Emergency Room will obtain patient consent. Enrolled patients will be assigned the next available treatment number and corresponding treatment. The physician via infusion pump will administer the study treatment. Data collection before, during, and after treatment, may be done by physician or nursing staff. Study data forms will be placed in opaque envelopes labeled "Mg/HA study" and placed in the secure drug cabinet. Study investigators (Coomes and Valrey) will periodically collect the data sheets and compile the data.

**Progress:** 15 subjects were enrolled onto this protocol during FY00. No adverse events have been reported and subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/020	<b>Status:</b> Ongoing
<b>Title:</b> A Model for Prehospital 12-Lead Acquisition Without A Dedicated 12-Lead ECG Machine		
<b>Principal Investigator:</b> Steven A. Pace, MD		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Fritz P. Fuller, N.R.E.M.T.-P; COL Alice M. Mascette, MC		
<b>Start Date:</b> 2/21/1997	<b>Est. Completion Date:</b> May 96	<b>Periodic Review:</b> 3/28/2000

**Study Objective:** To verify that a 12-lead ECG obtained with a cardiac monitor/defibrillation unit is comparable in accuracy to that of a dedicated 12-lead ECG machine.

**Technical Approach:** The management of ischemic chest pain and acute myocardial infarction hinges on early diagnosis and treatment with thrombolytic agents if indicated. It has been shown that prehospital recognition of acute MI using 12-lead electrocardiography and interpreted by nurses/paramedics trained in ECG evaluation can result in significantly faster times to thrombolytics compared to patients who did not receive a prehospital ECG. Today there are several portable 12-lead machines with computer assisted diagnosis available, but they have only recently become available and are very expensive. By utilizing a portable 12-lead machine (Lifepak 10) and demonstrating that it can produce diagnostic quality ECG's, we hope to make available to a large group of prehospital providers 12-lead capability without an increased monetary investment.

**Progress:** All data for this protocol has been collected and is being analyzed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/002	<b>Status:</b> Ongoing
<b>Title:</b> Emergency Surgical Procedures Laboratory Training Using the Goat ( <i>Capra hircus</i> )		
<b>Principal Investigator:</b> Steven A. Pace, MD		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Nathan T. Rudman, MC; MAJ James T. Vandenberg, MC; CPT Garrett R. Baer, SP		
<b>Start Date:</b> 10/17/1997	<b>Est. Completion Date:</b> Oct 00	<b>Periodic Review:</b> 10/28/1999

**Study Objective:** The objectives of this training exercise are to teach physicians one safe method of performing six life-saving procedures for trauma patients.

**Technical Approach:** The procedures listed below will be performed under the supervision of a staff member and the veterinarian assigned to Clinical Investigation. All animals will be anesthetized and then will be sacrificed immediately after the procedures. The procedures consist of 1) Chest tube insertion, 2) Thoracotomy, 3) Pericardiocentesis, 4) Diagnostic peritoneal lavage, 5) Venous cutdown, 6) Cricothyroidotomy

**Progress:** Four investigators received training during FY00 for a total of 10 trained overall. No adverse events were reported.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/028	<b>Status:</b> Ongoing
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret ( <i>Mustela putorius furo</i> ) Model		
<b>Principal Investigator:</b> Steven A. Pace, MD		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Daniel Mcilmail, MC; MAJ Nathan T. Rudman, MC; MAJ James T. Vandenberg, MC; LTC Mary P. Fairchok, MC		
<b>Start Date:</b> 12/18/1997	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> N/A

**Study Objective:** To improve the skill of physicians and other health care providers in pediatric endotracheal intubation, thereby improving the outcome of pediatric patients they treat.

**Technical Approach:** Ferrets will be anesthetized and course participants will be given the opportunity to intubate a ferret employing a laryngoscope and endotracheal tube. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure.

**Progress:** Two training sessions were held during FY00, training a total of 60+ nurses, pediatrics residents, and ER staff.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 99/105                      **Status:** Terminated

**Title:** A Double-blind, Randomized, Placebo-controlled Trial of a Tablet Formulation of Pleconaril in the Treatment of Viral Respiratory Infection

**Principal Investigator:** Steven A. Pace, MD

**Department:** Emergency Medicine

**Facility:** MAMC

**Associate Investigator(s):** MAJ James Terrio, MC; CPT Leah P. McMann, MC; Shirley Newcomb, BSN, MPH

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
May 00

**Periodic Review:**  
N/A

**Study Objective:** To determine the therapeutic effect of pleconaril on the time to complete resolution of all symptoms of VRI. Complete resolution is defined as a total score of 0 for 24 hours with no subsequent relapse of symptoms.

**Technical Approach:** This double-blind, placebo-controlled, randomized study will evaluate and compare a Placinoral tablet dosage regimen to matching placebo therapy on the reduction of the duration and severity of viral respiratory tract symptoms in adults presenting to ambulatory care or emergency medical clinics for treatment. The study will be conducted at approximately 100 centers throughout the US and Canada. Approximately 810 patients with suspected picornaviral respiratory infection will be randomized to receive Placinoral 400 mg t.i.d. or placebo t.i.d. for 7 days. Randomization will be stratified by smoking status. A nasal mucus sample will be collected at baseline for the determination of picornavirus by RT-PCR (patients discharge nasal mucus into a plastic sheet and the mucus is transferred to sample collecting tube).

Patients meeting the entrance criteria will receive their first dose of study drug immediately following signing the informed consent statement. The time of the first dose must be no more than 36 hours after onset of the first symptom of scoring system. Patients will continue the dosing regimen for the next 7 days after enrollment. A total of 21 doses will be administered to each study participant and the first 3 doses must be administered during the first 24 hours after randomization. Patients will be assigned blister packs of the study medication upon enrollment and will be carefully instructed on proper dosing. Subjects will record their symptoms, activity and concomitant medication use twice daily (midday and evening) in the diary. Patients will be contacted every other day preferably by the same person, until they are discharged from the study or have complete resolution of all symptoms. Patients will be discharged from the study on Day 21 and advised to return to the clinic for further evaluation if symptoms occur beyond this point. Symptomatic patients will remain under observation for as long as is judged necessary by the investigator for purposes of the study. The Biostatistics department of ViroPharma Incorporated will analyze the data of this study.

**Progress:** This protocol was terminated by the sponsor prior to final IRB approval at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/022	<b>Status:</b> Completed
<b>Title:</b> Comparison of Rectal and Temporal Thermometry in the Determination of Temperature in Children		
<b>Principal Investigator:</b> Janet H. Shotwell, M.D.		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ David A. Della-Giustina, MC; Thomas P. Boyer, DO; CPT Carolyn Warner, MC; MAJ Karen L. Della-Giustina, MC		
<b>Start Date:</b> 11/19/1999	<b>Est. Completion Date:</b> Dec 99	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if temporal thermometry is accurate in determination of temperature in children.

**Technical Approach:** This study evaluates the efficacy of new thermometers which are applied to the skin of the forehead compared to rectal temperature readings in children 0 - 3 years old. By directly comparing the readings, it will be determined if the new thermometers are useful tools to be used in treating children or if the traditional method of rectal thermometry is still the best indicator of temperature in children.

**Progress:** 430 patients were enrolled during FY00, with no adverse events reported. Statistical analysis has not yet been completed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/007

**Status:** Ongoing

**Title:** Is There Any Additional Efficacy in Adding Single Dose Intravenous Antibiotic Therapy to an Oral Antibiotic Regimen for Uncomplicated Cellulitis?

**Principal Investigator:** MAJ David A. Siegel, MC

**Department:** Emergency Medicine

**Facility:** MAMC

**Associate Investigator(s):** CPT Thomas R. Coomes, MC; MAJ Danny O. Stene, MC; CPT John Westhoff, MC; Janet H. Shotwell, M.D.; MAJ Robert W. Desverreaux, MC

**Start Date:**  
10/26/1999

**Est. Completion Date:**  
Nov 02

**Periodic Review:**  
N/A

**Study Objective:** To determine if there is any additional efficacy in adding single dose intravenous antibiotic therapy to an oral antibiotic regimen for uncomplicated cellulitis.

**Technical Approach:** Subjects with cellulitis will be enrolled and randomly assigned into one of two treatment arms. The first arm will receive intravenous cefazolin, and the second arm will receive a parenteral placebo. All subjects will receive a 10-day course of oral cephalexin. Clinical indicators will be assessed and compared at days 7 and 14.

**Progress:** 22 patients have been enrolled in this study in FY00 at MAMC. No adverse events have been noted by the DEM staff. Patient enrollment continues.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/059	<b>Status:</b> Completed
<b>Title:</b> Emergency Medicine Residents' Attitudes Towards Chemical/Biological/Nuclear Accident Education and Knowledge of Casualty Management			
<b>Principal Investigator:</b> MAJ David A. Siegel, MC			
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Bradley N. Younggren, MC			
<b>Start Date:</b> 4/25/2000	<b>Est. Completion Date:</b> May 00		<b>Periodic Review:</b> N/A

**Study Objective:** Test emergency medicine residents' basic knowledge in chemical, biological, and nuclear casualty management and gather information of emergency medicine residents' attitudes concerning training in the field of chemical/biological/nuclear terrorism, in order to ultimately standardize the mechanism in which the training is executed.

**Technical Approach:** This protocol developed a survey to estimate emergency medicine residents' knowledge in the field of nuclear, biological, and chemical warfare casualty management, as well as gain an understanding of residents' expectations for training during their residency. The surveys are to be administered anonymously to residents in seven different emergency medicine programs and returned to the study investigator. Results are to be compiled to identify both areas of weakness in residents' knowledge and residents' appraisals of teaching methods currently in use.

**Progress:** 70 surveys have been returned (68%) and results have been finalized. The final manuscript is currently being prepared and is not available at the time of this report.

### Detail Summary Sheet

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<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/080	<b>Status:</b> Ongoing
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**Title:** Impact of Chest Radiography Results on Clinician Decision-making for Young Adult Patients Presenting to the Emergency Department with Non-traumatic Anterior Chest Pain, Normal Vital Signs and a Normal Physical Exam

**Principal Investigator:** Marcus A. Trione, M.D.

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**Department:** Emergency Medicine

**Facility:** MAMC

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**Associate Investigator(s):** MAJ David A. Della-Giustina, MC; CPT Walter A. Fink, Jr., MC; MAJ Robert K. Lather, MC

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**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 01

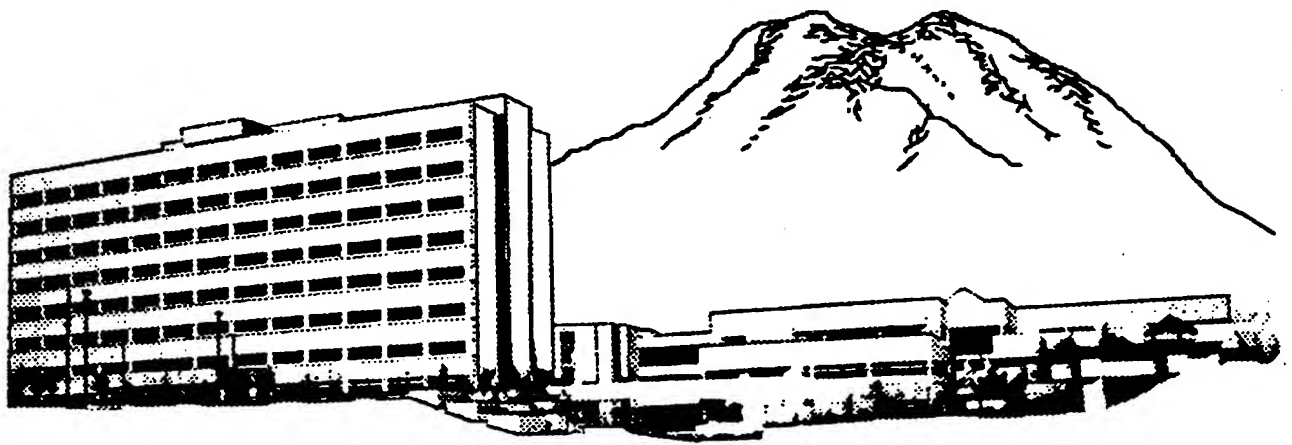
**Periodic Review:**  
N/A

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**Study Objective:** The purpose of this study is to evaluate the impact of chest radiography on clinical decision-making in young adult patients presenting to an Emergency Department with non-traumatic anterior chest pain, normal vital signs and a normal physical exam.

**Technical Approach:** This study will be a prospective evaluation of clinical decision making by ED physicians. Physicians will be asked to present a pretest diagnosis and treatment plan with disposition prior to interpreting the chest radiograph. Diagnosis and treatment plan will then be assessed in light of the chest radiograph. Finally, the physician will be asked to assess whether the chest radiograph altered the patient's diagnosis or treatment plan. For both diagnosis and treatment, the physician will be asked to classify the change from pre- to post-interpretation as incidental or major. This study's goal is to assist in the generation of rational, evidence-based guidelines for the use of chest radiography in this low-risk (military) population.

**Progress:** 32 subjects have been enrolled in this study in FY 00 at MAMC. Enrollment will continue with the expected goal of 250 patients, extending the previously anticipated end date until possibly 2002.



## Detail Summary Sheets

Department of Family Practice

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/098      **Status:** Completed

**Title:** Can An Instructional Video Improve the Quality of Cervical Cytological Smears in A Family Practice Residency

**Principal Investigator:** LTC Gary W. Clark, MC

**Department:** Family Practice

**Facility:** MAMC

**Associate Investigator(s):** COL Joseph F. Yetter III, MC

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
Aug 00

**Periodic Review:**  
N/A

**Study Objective:** (1) To determine if the rate of limited cervical smears can be reduced through the use of an instructional video and (2) to determine if the instructional video would be an acceptable tool to be used by family practice and OB/GYN providers either for resident education or continuing quality improvement.

**Technical Approach:** This study examines the acceptability of the instructional video to the family practice and OB/GYN providers of MAMC. In addition providers will be asked to suggest how to best use the video. Providers from both clinics will be shown the video and asked to fill out a brief survey. The results of the survey will be reported using simple descriptive statistics.

**Progress:** The video was shown to 30 individuals consisting of 4 medical students, one PA student, 2 nurse practitioners, 2 PAs, 2 interns, 2 second year FP residents, 5 third year FP residents, and 12 FP staff. The study group included 21 males and 9 females. The participants were asked to fill out a survey immediately after viewing the video. Results: Most providers (94%) found that the technique demonstrated resembled the technique that they were currently using. All participants agreed that the video would be useful to teach residents and students how to do a cervical smear. 94% of the providers felt that the video would be useful if shown as part of their departments continuing quality improvement program. Conclusion: The instructional video is a good tool for teaching residents and students how to perform a pap smear and may be useful in the CQI process as well. The video should be shown both during new intern orientation and yearly, as part of the weekly lecture series. Some improvements to the video can be made to make it more pleasing to view and to provide references about the evidence supporting the method used.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/107

**Status:** Ongoing

**Title:** Prevention of Unintended Pregnancy in the Military: A Multicenter Randomized Clinical Trial

**Principal Investigator:** MAJ Diane M. Flynn, MC

**Department:** Family Practice

**Facility:** MAMC

**Associate Investigator(s):** LTC Jeffrey Clark, MC; COL Jeffrey D. Gunzenhauser, MC; COL Roderick F. Hume, MC; Ann K. Lancaster, CHN; MAJ Wanda A. Barfield, MC; MAJ Sherri Baker, AN

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Dec 04

**Periodic Review:**  
N/A

**Study Objective:** To determine if a 3-hour educational class coupled with a system of facilitated access to health care are an effective strategy to: (1) Decrease the rate of unintended pregnancies among military women ages 18-25, (2) Decrease the rate of unintended paternity among military men ages 18-25, and (3) Advance the stage of behavioral change with respect to contraceptive attitudes among military men and women ages 18-25.

**Technical Approach:** Subjects will be given a questionnaire to determine their attitudes about pregnancy and/or paternity. Subjects will then attend a 3-hour class on reproductive health. After one year, class participants will be again fill out a questionnaire to determine rates of pregnancy/paternity in the previous year and about the outcomes of those pregnancies. Questionnaires will also ask about contraceptive use and behavioral stages of change with regard to contraceptive attitudes.

**Progress:** This protocol recently received IRB review and approval. The protocol will not proceed until adequate funding is secured.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 97/050	<b>Status:</b> Ongoing
<b>Title:</b> Unintended Pregnancy Prevention Program			
<b>Principal Investigator:</b> MAJ Diane M. Flynn, MC			
<b>Department:</b> Family Practice		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Jeffrey D. Gunzenhauser, MC; COL Roderick F. Hume, MC; Ann K. Lancaster, CHN; LTC Jeffrey B. Clark, MC			
<b>Start Date:</b> 2/21/1997	<b>Est. Completion Date:</b> Mar 97		<b>Periodic Review:</b> 2/23/1999

**Study Objective:** The purpose of this study is to evaluate the effect of an intervention consisting of education and facilitated access to contraception on the unintended pregnancy rate of active duty US Army soldiers serving at Ft Lewis, WA.

**Technical Approach:** This research project is a randomized clinical trial designed to determine the effect of education and facilitated access to contraception on unintended pregnancy rates among female soldiers at Ft Lewis. Effectiveness of the intervention will be determined by: 1) Calculating annualized pregnancy rates using SIDPERS data and positive beta-HCG results from the MAMC clinical laboratory; unintended pregnancy rates will be determined from a survey completed at prenatal care orientation. 2) A questionnaire mailed to women in the Intervention Group and the Control Group one year after the intervention designed to assess contraception use, whether the intervention affected contraception use, and the rate of unintended pregnancy.

**Progress:** Data analysis has been completed for two of three outcomes for the UPPP. (1) Among female soldiers who presented to MAMC for prenatal care one year after program implementation, the rate of unintended pregnancy was compared between women who received the intervention with those who did not, (Relative risk 1.1). (2) Among women who had positive pregnancy tests at MAMC lab, the rate of unintended pregnancy was compared between women from units who received the intervention and those who did not. (No significant difference.) (3) Data analysis remaining includes analysis of responses to mailed surveys administered one year after program implementation.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/067	<b>Status:</b> Ongoing
<b>Title:</b> Effects of the Acetic Acid Wash on the Cytologic Interpretation of the PAP Smear		
<b>Principal Investigator:</b> CPT Mary V. Krueger, MC		
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Brian C. Harrington, MC; CPT Robert H. G. Holland, MC; COL Mark E. Potter, MC; CPT Veronica Santee, MC		
<b>Start Date:</b> 4/27/1999	<b>Est. Completion Date:</b> Sep 99	<b>Periodic Review:</b> 11/28/2000

**Study Objective:** To determine if interpretation of cervical intraepithelial neoplasia is altered by applying acetic acid prior to taking the Pap smear during colposcopic examination.

**Technical Approach:** Premenopausal, nonpregnant females with abnormal Pap smears (ASCUS or higher grade) presenting for first time colposcopy within 6 months in Family Practice and OB/GYN clinics at Madigan who agree to participate in the study will be stratified based on presenting Pap diagnosis (ASCUS, LGSIL, HGSIL), then randomized to the saline (Group 1) or acetic acid (Group2) groups. Each group will have a Pap smear done: after saline washing in Group 1, and after acetic acid washing in Group 2. The cytologist will be blinded to the use of saline vs acetic acid for the wash. Cytologic diagnoses will be based on the Bethesda criteria. We will compare the results between the saline and acetic wash groups to assess whether acetic acid changes the diagnosis, specificity, and/or increases the number and/or grade of abnormal slides.

**Progress:** A change of PI was approved due to the PCS of the original PI. 26 subjects have been enrolled in FY00 at MAMC. This study remains ongoing for subject enrollment.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/020	<b>Status:</b> Completed
<b>Title:</b> Assessing the Stages of Change for Contraceptive Use in the Prevention of Pregnancy and Sexually Transmitted Disease		
<b>Principal Investigator:</b> CPT Jennifer H. Potter, MC		
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Diane M. Flynn, MC; COL Roderick F. Hume, MC; COL Jeffrey D. Gunzenhauser, MC; LTC Gary W. Clark, MC		
<b>Start Date:</b> 12/15/1998	<b>Est. Completion Date:</b> May 99	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the effect of the unintended pregnancy prevention program on the stage of change of AD women with regard to contraceptive behavior.

**Technical Approach:** This is a prospective controlled study to assess the stages of change of 600 AD soldiers regarding contraceptive use in the prevention of unintended pregnancy and sexually transmitted disease. Questionnaires will be given to the study group before and after the UPPP intervention. It will also be given to a group who has not received the class at the same time interval to act as a comparison group. Dependent variable consist of the study group, the control group and the age/rank/gender of group participants. Analysis will be chi-square to (1) compare the study group's incidence of change to the control group's incidence of change regarding contraceptive behavior, (2) compare the incidence of change within the study group before and after the intervention. The five different stages of change will also be converted to numerical rank to compare the mean ranks by group and by age/rank of participants using 2-factor analysis of variance.

**Progress:** Of the 108 males and 57 females surveyed, 82% responded that they were not planning pregnancy in the next year. Regarding pregnancy prevention, most service members (70% of women and 59% of men) were in the maintenance phase of change. No statistically significant advancement was noted in either men or women after the intervention. However, there was a trend toward a more advanced stage of change with regard to prevention of sexually transmitted disease. In conclusion, assessing the stage of change is a strategy that family physicians can use to promote healthy behaviors. This study yielded valuable descriptive data on the baseline stage of change of a military population with regard to unintended pregnancy and sexually transmitted disease prevention. It will allow future interventions to focus on subgroups most likely to benefit.



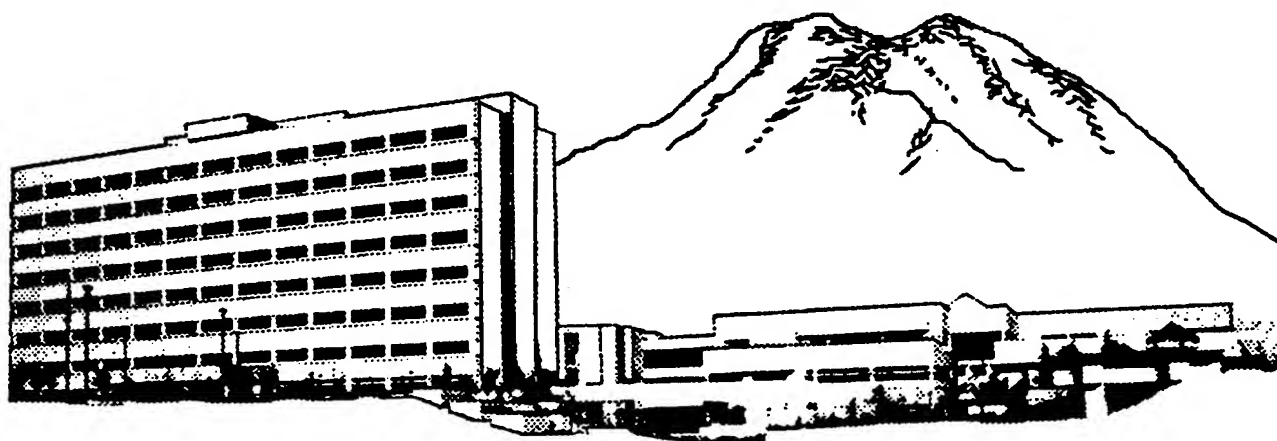
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/025	<b>Status:</b> Completed
<b>Title:</b> Biomedical Ethics Core Curriculum: MAMC & AMEDD?		
<b>Principal Investigator:</b> MAJ Keith L. Salzman, MC		
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Joseph F. Yetter III, MC; Ann Downer, PhED; Nancy Stevens, M.D., MPH		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Jul 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if an intranet computer based training module can be successfully used in a major medical center in order for the DoD Military Health System to meet the ethical educational goals established by ACGME, JCAHO, CIRO, etc.

**Technical Approach:** This study will design and implement an interactive computer-based training model for medical ethics.

**Progress:** The interactive, computer based training model for biomedical ethics was designed and produced over the last year. It has approval from CME and CHE. It is currently being produced by AVO for release on the Madigan Army Medical Center Intranet.



## Detail Summary Sheets

Cardiology Service,  
Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/062	<b>Status:</b> Ongoing
<b>Title:</b> Substudy 02: The Neurohormone Substudy of a Multinational, Multicenter, Double-blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-term Treatment with Valsartan, Captopril, and Their Combination in High-risk Patients After Myocardial Infarction		
<b>Principal Investigator:</b> LTC James J. King, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David T. Schachter, MC; LTC Michael Wilson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC		
<b>Start Date:</b> 4/25/2000	<b>Est. Completion Date:</b> Apr 03	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the effect of valsartan, captopril, and the combination of valsartan and captopril on the levels of neurohormones, measures of oxidative stress, and inflammation (plasma catecholamines, aldosterone, brain natriuretic peptide, aldehydes, adrenomedullin, collagen one telopeptide, procollagen type III, Nterminal propeptide, and C-reactive protein) at baseline, one month and 20 months post infarction, and with each episode of congestive heart failure requiring hospitalization and to assess the relationships between post-infarction neurohormonal activation, cardiovascular risk factors, and clinical outcome and evaluate the effect of valsartan, captopril and their combination on these relationships.

**Technical Approach:** This substudy of the original VALIANT (Valsartan and Captopril) study will look at the presence of neurohormones as an indicator of prognosis for patients suffering from myocardial infarction. Blood samples will be taken at baseline (before initial dose of VALIANT study drug), at one month, and again at twenty months. Additionally, blood samples will be taken whenever the patient is hospitalized for heart failure. Samples will be sent to a central laboratory for evaluation.

**Progress:** One patient was enrolled in this substudy in FY00 at MAMC. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/063	<b>Status:</b> Ongoing
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**Title:** Substudy 04: The Microalbuminuria Substudy of a Multinational, Multicenter, Double-blind, Randomized, Active Controlled, Parallel Group Study Comparing the Efficacy and Safety of Long-term Treatment with Valsartan, Captopril, and Their Combination in High-risk Patients After Myocardial Infarction

**Principal Investigator:** LTC James J. King, MC

<b>Department:</b> Medicine/Cardiology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC David T. Schachter, MC; LTC Michael J. Wilson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC

**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Apr 03

**Periodic Review:**  
N/A

**Study Objective:** To assess the relationship between microalbuminuria and prognosis, and evaluate how valsartan and captopril modify this relationship and whether a correlation between microalbuminuria, neurohormonal activation and gene polymorphisms exists.

**Technical Approach:** This substudy of the original VALIANT (Valsartan and Captopril) study will look at the presence of albuminuria as an indicator of prognosis for patients suffering from myocardial infarction. Spot urine samples will be taken at baseline (before initial dose of VALIANT study drug), at one month, and again at twenty months. Additionally, urine samples will be taken whenever the patient is hospitalized for heart failure. Urine samples will be sent to a central laboratory for evaluation.

**Progress:** One patient was enrolled in this substudy in FY00 at MAMC. Patient enrollment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/099

**Status:** Ongoing

**Title:** A Phase IIb, Randomized, Open Label Trial with 3 Parallel Groups, Full Dose TNK-tPA Together with Heparin Sodium, Full Dose TNK-tPA Together with Enoxaparin and Half Dose TNK-tPA with Abciximab and Heparin Sodium in Patients with Acute Myocardial Infarction, Protocol 1123.10

**Principal Investigator:** LTC James J. King, MC

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Associate Investigator(s):** LTC David T. Schachter, MC; LTC Michael J. Wilson, MC; MAJ Rosemary P. Peterson, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Apr 01

**Periodic Review:**  
N/A

**Study Objective:** The objective of this study is to evaluate the safety and efficacy of full dose TNK-tPA with heparin sodium (Group A), full dose TNK-tPA combined with enoxaparin (Group B), and half dose TNK-tPA combined with abciximab and heparin sodium (Group C).

**Technical Approach:** After obtaining informed consent, eligible subjects will be randomized into one of three groups; Group A will receive TNK-tPA (full dose) and heparin sodium (unfractionated heparin, Group B will receive TNK-tPA (full dose) and enoxaparin (low molecular weight heparin) and Group C will receive TNK-tPA (half dose) and abciximab and low dose heparin sodium (unfractionated heparin). Subjects will be contacted or return to the hospital for follow-up at 30 days for vital status and clinical outcome. One year after randomization, subjects will be contacted by phone or mail to check their vital status. The satellite study will not be initiated at MAMC.

**Progress:** This study recently received final IRB approval. No work has been initiated on this study in FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/042		<b>Status:</b> Ongoing	
<b>Title:</b> The Coreg Heart Failure Registry: COHERE					
<b>Principal Investigator:</b> LTC James J. King, MC					
<b>Department:</b> Medicine/Cardiology				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ James P. Olson, MC; MAJ Rosemary P. Peterson, MC; MAJ Michael L. Yandel, MC					
<b>Start Date:</b> 2/23/1999		<b>Est. Completion Date:</b> Jun 99		<b>Periodic Review:</b> 4/25/2000	

**Study Objective:** (1) To collect clinically pertinent outcome data (e.g., mortality, need for hospitalization, use of concomitant medications, patient global assessment, NYHA class in patients with heart failure) receiving Coreg under the care of a broad population of community physicians, (2) To compare the clinical characteristics of the patients treated in the US Phase III and early extended physician use programs with those treated in the community and to assess outcome differences in major subpopulations, (3) To characterize the experience with initiation of Coreg in the community, and (4) To compare patient characteristics and management approaches between cardiologists and internists.

**Technical Approach:** The Coreg Heart Failure Registry will document the relationship of selected patient characteristics to outcomes, such as morbidity, mortality, need for hospitalizations, quality of life and change in clinical status as well as tolerability. By the year 2000, COHERE will contain the most up-to-date information on the natural history of, and effect of B-Blockade in CHF. COHERE will involve approximately 600 participating physicians, and will enroll 6,000 patients with heart failure receiving Coreg. The live portion of the registry will take place over 30 months, and patients will be assessed over a period of 24 months.

**Progress:** 18 patients were enrolled in FY00, 2 in FY99, for a total of 20 patients enrolled at MAMC. No further enrollment is planned at this time. No adverse events have been reported. Patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/053

**Status:** Ongoing

**Title:** Multinational, Multicenter, Double-Blind, Randomized, Active Controlled, Parallel Group Study Compring the Efficacy and Safety of Long-Term Treatment with Valsartan, Captopril, and Their Combination in High-Risk Patients After Myocardial Infarction

**Principal Investigator:** LTC James J. King, MC

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Associate Investigator(s):** COL Alice M. Mascette, MC; MAJ James P. Olson, MC; LTC David T. Schachter, MC; CPT Kenneth M. LeClerc, MC; MAJ Steven E. Miller, MC; LTC Michael J. Wilson, MC

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Apr 03

**Periodic Review:**  
3/28/2000

**Study Objective:** (1) To demonstrate that long-term administration of valsartan is more effective than captopril in reducing total mortality after acute myocardial infarction, (2) To demonstrate that long-term administration of the combination of valsartan with captopril is more effective than captopril alone in reducing total mortality after acute myocardial infarction, and (3) If valsartan as monotherapy cannot be shown to be superior to captopril as in objective 1, to demonstrate that long-term administration of valsartan given as monotherapy is at least as effective as captopril given as monotherapy in reducing total mortality after acute myocardial infarction.

**Technical Approach:** VALIANT is a prospective multinational, multicenter, double-blind, randomized, active-controlled phase III study with three parallel treatment groups. The three treatment groups are 1) Captopril monotherapy (active control drug). The target dose is 50 mg three times daily; 2) Valsartan monotherapy (investigational drug). The target dose is 160 mg twice daily; 3) The combination of captopril and valsartan (investigational regimen). The target doses are 50 mg three times daily and 80 mg twice daily, respectively. The study consists of two phases: 1) a study medication initiation and titration phase and 2) maintenance phase. The duration of these two phases depends upon the patient's status and response to study medication. Randomization and initiation of study medication will occur at Visit 1 on Day 1. For most patients, this will occur in hospital. Dose titration and maintenance will occur at Visits 2-16. Visit 2 will occur on Day 15 or at hospital discharge, whichever is first. For patients not in hospital at the time of randomization, Visit 2 will occur on Day 15. Visits 3-16 are planned as outpatient visits, but depending on the patient's status, may occur in hospital. They are to be performed at specified time points but some flexibility is allowed. During the first year, visit may take place up to 15 days before or after the protocol-scheduled visit. Telephone follow-up is permitted if the patient cannot come for follow-up visits. The study will end when the required number of primary endpoints has been reached. This may occur prior to or after Month 48. If the study ends prior to Month 48, the procedures listed for Visit 16 will be completed for all patients. If the study is extended beyond Month 48, the procedures listed for Visit 15 will be completed every 4 months until study end, at which point the procedures listed for Visit 16 will be completed.

**Progress:** Five patients have been enrolled in this study in FY00 at MAMC and continue to be followed. All serious adverse events have been reported to the IRB; none occurred at MAMC. Patient complaints include dry cough, back pain, viral cold symptoms and acute bronchitis; however, none of these are thought to be related to their study participation. Patient enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/013	<b>Status:</b> Ongoing
<b>Title:</b> Magnesium in Coronaries (MAGIC): A Study of the Effect of Magnesium Administration in Patients with Acute Myocardial Infarction		
<b>Principal Investigator:</b> LTC David T. Schachter, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC James J. King, MC		
<b>Start Date:</b> 12/15/1998	<b>Est. Completion Date:</b> Mar 01	<b>Periodic Review:</b> 12/15/1999

**Study Objective:** To determine if administration of intravenous magnesium within 6 hours of symptom onset in high-risk patients with suspected acute MI reduces all cause and 30-day mortality.

**Technical Approach:** Subjects will be randomly assigned study drug or placebo in a double-blinded fashion. Subjects will be stratified by site, and by whether the subject is eligible for reperfusion therapy or not. Stratum I will include subjects who are 65 years or older and are eligible for reperfusion therapy. Stratum II will include patients of any age who are not eligible for reperfusion therapy. Subjects will receive either magnesium sulfate or placebo by bolus followed by 24 hour continuous infusion. Follow-up evaluation by telephone or clinic visit will be performed by the PI. The primary endpoint is 30-day all cause mortality. Secondary endpoints include (1) use of intravenous inotropic therapy and/or vasopressors and/or mechanical support for a failing circulation (IABP, LVAD), (2) electrical reversion of ventricular fibrillation or sustained ventricular tachycardia, and (3) placement of an external or transvenous pacemaker.

**Progress:** Three patients entered this study in FY99, three patients enrolled in FY00, for a total of 6 patients. This study remains ongoing for further patient enrollment at MAMC.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/110

**Status:** Ongoing

**Title:** Efficacy and Safety Study of the Oral Direct Thrombin Inhibitor H 376/95 Compared with Dose-adjusted Warfarin (Coumadin) in the Prevention of Stroke and Systemic Embolic Events in Patients with Atrial Fibrillation (SPORTIF V)

**Principal Investigator:** LTC Michael J. Wilson, MC

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Associate Investigator(s):** LTC David T. Schachter, MC; LTC James J. King, MC; MAJ Rosemary P. Peterson, MC; COL Frederick G. Flynn, MC

**Start Date:**  
7/25/2000

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
N/A

**Study Objective:** (1) To determine whether H 376/95 is non-inferior compared to dose-adjusted warfarin aiming for an INR 2.0-3.0 for the prevention of all strokes (fatal and nonfatal) and systemic embolic events in patients with chronic non-valvular AF, (2) To compare the efficacy of H 376/95 to that of dose-adjusted warfarin aiming for an INR of 2.0-3.0 for the combined endpoint of prevention of death, nonfatal strokes, nonfatal systemic embolic events and nonfatal acute myocardial infarction (AMI), (2) To compare the efficacy of H 376/95 to that of dose-adjusted warfarin aiming for INR 2.0-3.0 for the combined endpoint of prevention of ischemic strokes, TIAs and systemic embolic events, and (3) To assess the safety of H 376/95 compared to dose-adjusted warfarin aiming for INR 2.0-3.0 with an emphasis on major and minor bleeding events and any treatment discontinuations.

**Technical Approach:** This is a multicenter, randomized, double-blind, two arm, parallel group study comparing the effects of H 376/95 versus dose-adjusted warfarin. Subjects will be followed for at least one year, up to 2 1/2 years. Eligible patients will be randomized and stratified according to current low dose aspirin use and previous stroke or TIA history. Subjects will complete a 2 week screening period prior to randomization to receive either H 376/95 36 mg bid (and placebo for warfarin) or to dose-adjusted warfarin od (and placebo for H 376/95). Screening will include consent process, medical history, vital signs, ECG, blood/urine samples and physical examination. Upon randomization, a second ECG will be performed, and the Stroke Symptom Questionnaire will be completed. Study visits will be performed at weeks 1, 4, 6, and then months 2, 3, 4, 5, 7, 8, 10, 12 and then every 3 months thereafter until the study treatment is completed. At study visits, study medication will be returned and new drug will be dispensed, concomitant medications and adverse events will be reviewed, safety blood samples and melagatran samples will be obtained. INR samples will be obtained as necessary. At months 6, 12, 18, and 24 visits subjects will undergo the above tests in addition to ECGs and the Stroke Symptom Questionnaire. Subjects will be contacted by telephone at months 7, 9, and 11 and will be required to return to the clinic for in-clinic INR evaluation as necessary. At the end of the study subjects will have a complete PE, vital signs, ECG, blood tests, INR samples, and the Stroke Symptom Questionnaire will be obtained. Following treatment withdrawal, the subjects will be followed an additional 2 weeks until satisfactory conversion from blinded study therapy to normal active treatment has been made. Subjects will return to the clinic for INR draws using a sponsor provided CoaguChek System. INR values will remain blinded to the investigator and study coordinator utilizing the CoaguChek System and the IVRS system.

**Progress:** This study recently received IRB review and approval; however, final approval has not yet been granted. The study continues to be on hold until impact statements are received from other departments/services. No work has been initiated on this study in FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 96/069      **Status:** Ongoing

**Title:** Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

**Principal Investigator:** LTC Michael J. Wilson, MC

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick A. Cambier, MC; COL Roger F. Chamusco, MC; COL Alice M. Mascette, MC; MAJ Herman E. Collier III, MC; LTC Karl C. Stajduhar, MC; MAJ Michael D. Eisenhauer, MC; CPT John A. McHenry, MC; MAJ Maureen A. Arendt, MC; CPT Thomas M. Roe, MC; MAJ James P. Olson, MC

**Start Date:**  
2/16/1996

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
1/25/2000

**Study Objective:** 1) To compare whether optimized antiarrhythmic drug therapy administered to attempt to maintain sinus rhythm has an impact on total mortality when compared to optimized therapy which controls the heart rate. 2) Since stroke is such an important endpoint in trials of patients with atrial fibrillation, composite endpoints will include the following: total mortality, disabling stroke or anoxic encephalopathy, major bleeding and cardiac arrest; cost; quality of life.

**Technical Approach:** This is a multi center trial sponsored by the National Heart, Lung, and Blood Institute. The purpose is to compare the effect on survival of two different treatment plans in patients with atrial fibrillation. One treatment is aimed at rate control and the other at maintaining a normal sinus rhythm. The primary physician will choose which drug or drugs are used to obtain each treatment objective. The physician will initially determine the treatment to convert patients to normal sinus rhythm after which the patient will be randomized to one of the treatments described above. Patients will be followed at month 2 and 4 and then at least every 4 months until the year 2001. Patients will complete a quality of life questionnaire and have an assessment of their functional status completed at various time points. Patients who fail their assigned treatment or are intolerant will continue to be followed regardless of crossover to another therapy. We anticipate enrolling 15 patients at Madigan Army Medical Center.

**Progress:** Four patients were enrolled during FY 00 for a total of 32 patients enrolled. During FY00, one patient was lost to follow-up and 3 patients died. All serious adverse events have been reported to the IRB. This study is closed to patient entry, but remains ongoing for continued follow-up on 28 patients. LTC Michael Wilson assumed the role of PI, 15 Feb 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/140	<b>Status:</b> Ongoing
<b>Title:</b> A Double-Blind, Placebo-Controlled, Parallel Design Study to Determine the Effect of 100 mgs of Orally Administered Azimilide Dihydrochloride versus Placebo on Survival in Recent Post-Myocardial Infarction Patients at Risk of Sudden Death (ALIVE)		
<b>Principal Investigator:</b> LTC Michael J. Wilson, MC		
<b>Department:</b> Medicine/Cardiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Maureen A. Arendt, MC; MAJ Karen A. Hicks, MC; MAJ James P. Olson, MC; LTC James J. King, MC; LTC David T. Schachter, MC; CPT Kenneth M. LeClerc, MC; CPT Allan B. Wicks, MC; MAJ Steven E. Miller, MC; MAJ Theresa A. Horne, AN; COL Alice M. Mascette, MC; MAJ Michael L. Yandel, MC		
<b>Start Date:</b> 9/19/1997	<b>Est. Completion Date:</b> May 99	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** To evaluate the effects of 75 mg of azimilide dihydrochloride versus placebo or 100 mg of azimilide dihydrochloride versus placebo on all-cause mortality, based on longitudinal intent-to-treat observations in patients with a recent (within 6 to 21 days) acute MI, low left ventricular ejection fraction (15 to 35%), and low heart rate variability ( $\leq 20$  U). These patients are defined as "at high risk" of sudden death.

**Technical Approach:** This is a randomized, double-blind, placebo-controlled, multi-national study at approximately 500 study centers. A treatment regimen consisting of daily oral doses of 75 or 100 mg of azimilide dihydrochloride will be compared to a placebo group in a parallel design. Patients will be equally randomized across all 3 treatment groups. Patients who have recently experienced an acute MI and meet other study entrance and screening criteria will receive their first dose of study medication within 6-21 days of that MI. Once-daily treatment will be administered for approximately one year. No specific hospitalization is required for treatment. Screening procedures (to include a 24 hour Holter monitor) will be done to determine the group "at high risk" of sudden arrhythmic death. Evaluations during the treatment period will take place at Week 2, and at Months 1, 4, 8, and 12. Monthly serum pregnancy tests will be performed on females of childbearing potential who are not surgically sterile. Patients who complete 365 days of dosing will be followed for one month after completion of their participation in the study. Patients who withdraw from the trial early will return within 4 weeks for study exit procedures and furthermore, will be followed to assess survival status until the time at which they would have completed 365 day of dosing had they remained in the trial. Safety monitoring will include but is not limited to, clinical laboratory test results, 12-lead ECG measurements and frequency and severity of adverse events.

**Progress:** Three patients were enrolled onto this study during FY00 for a total of five patients enrolled at MAMC. One patient was withdrawn from the study prior to drug administration due to serious adverse event. All adverse events have been reported to the IRB. This study is closed to patient entry, but remains ongoing for continued patient follow-up. LTC Michael Wilson assumed the role of PI, 15 Feb 00.

### Detail Summary Sheet

Date: 29 Sep 00		Number: 99/055	Status: Completed
Title: Low Dose Niacin Supplementation with Chronic Statin Therapy			
Principal Investigator: CPT Jennifer S. Wink, MC			
Department: Medicine/Cardiology		Facility: MAMC	
Associate Investigator(s): LTC James J. King, MC; Rick Rutledge, R.Ph.; Larry W. Green, R.Ph.			
Start Date: 3/23/1999	Est. Completion Date: Dec 99	Periodic Review: 2/22/2000	

**Study Objective:** This study tests the hypothesis that very low dose Niacin will positively affect the lipid profile, by significantly raising high-density lipoprotein cholesterol levels.

**Technical Approach:** This study will be a randomized, double-blinded, placebo controlled study. 40-50 subjects will be recruited with 30 completing the study. They will receive either 50 mg BID niacin or placebo for 90 days. Other anti-lipid therapies will be stable. Neither the principal nor the associate investigators will be aware of randomization until analysis occurs at the end of the study. HDL, Lipids, glucose, LFT, TSH and electrolytes will be recorded at day 0 and day 90. A paired T-test will be used to compare HDL, Lipids, glucose, LFT, TSH and electrolytes levels.

**Progress:** 50 subjects on stable statin therapy for 3 months were consented in this study at MAMC and blindly randomized to either placebo or niacin 50 mg PI BID for 3 months. Results: 39 patients completed the study. Very low dose niacin added to statin therapy increased HDL (+2.1 mg/dL in niacin group vs. -0.56 mg/dL for placebo group,  $p=.0246$  by ANOVA). Five patients on niacin, vs. 2 patients on placebo, had episodes of flushing. None of the subjects halted study medication secondary to side effects, no major side effects were reported. Conclusions: The addition of very low dose niacin to statin therapy increased HDL cholesterol significantly, while avoiding the side effects that are associated with traditional doses of niacin therapy.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/036      **Status:** Completed

**Title:** Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure

**Principal Investigator:** MAJ Michael L. Yandel, MC

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Associate Investigator(s):** LTC James J. King, MC; MAJ James P. Olson, MC; LTC David T. Schachter, MC; MAJ Rosemary P. Peterson, MC

**Start Date:**  
2/23/1999

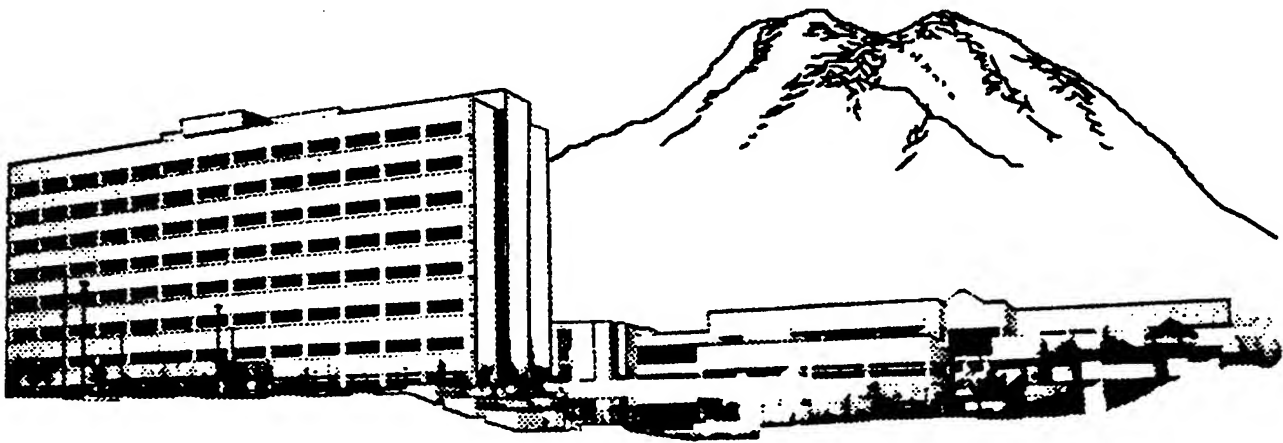
**Est. Completion Date:**  
Aug 99

**Periodic Review:**  
N/A

**Study Objective:** Primary objective of this study is to determine whether early interventional therapy with inodilator milrinone reduces the total number of days of hospitalization for cardiovascular events within 60 days following therapy. Secondary objectives: (1) reduces the proportion of treatment failures within the first 48 hours from randomization, (2) increases the proportion of patients achieving the target dose of ACE-inhibitor therapy and reduces the time to achieve target dose, (3) improves clinical outcome as measured by a patients visual analog scale and the overall personalized treatment effect questionnaire, measurements taken at admission, on discharge, day 30 and day 60, (4) improves heart failure score, measured at admission, day 3 and discharge, (5) reduces the length of initial hospitalization in number of days from the time of randomization to initial discharge, (6) reduces the number of days of hospitalization for primary cardiovascular disease post discharge and all cause admissions within 60 days following randomization, (7) reduces the number of days of hospitalization for cardiovascular events within 30 days of randomization, (8) influences the incidence of adverse events and (9) influences mortality.

**Technical Approach:** Subjects will be randomized within 48 hours of admission to receive either early intravenous milrinone therapy with conventional therapy and maintenance of oral therapy or early intravenous placebo with conventional therapy and maintenance of oral therapy (control care group). Study drug will be started at a dose of 0.5 mcg/kg/min without a loading dose and continued for a minimum of 24 hours. All efforts will be made to maintain the infusion for 48 hours and it may be maintained up to 72 hours at the discretion of the investigator. The control group will receive a placebo infusion. The heart failure score will be determined at day 3 and at discharge. Subjects will be seen (or telephone contact made) at 30 days and at 60 days following randomization.

**Progress:** This study was closed to patient entry, 22 Feb 00, by request of the study sponsor. One patient was consented at MAMC; however the patient died prior to study drug administration. This event was reported to the IRB, 13 Dec 99.



## Detail Summary Sheets

Dermatology Service,  
Department of Medicine

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/081

**Status:** Terminated

**Title:** A Randomized, Placebo-controlled, Multiple-dose, Double-blind Study of the Efficacy of Terbinafine HCl Cream, 1% for the Prophylactic Treatment of Tinea Pedis in Military Personnel

**Principal Investigator:** LTC Thomas K. Vaughan, MC

**Department:** Medicine/Dermatology

**Facility:** MAMC

**Associate Investigator(s):** CPT Irene M. Rosen, MC; CPT Robert C. Price, MC

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
N/A

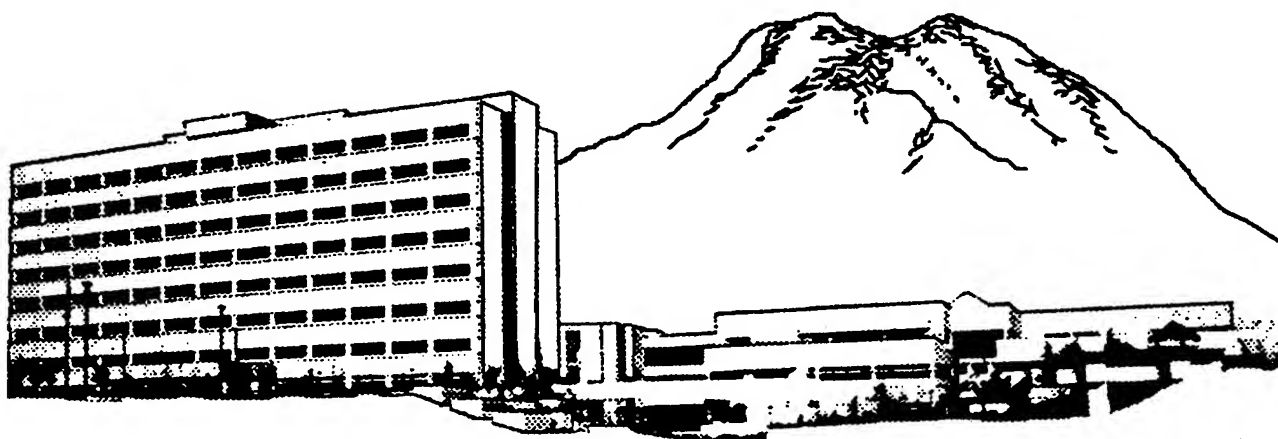
**Study Objective:** To determine whether terbinafine HCl cream, 1% when used once a day for seven consecutive days every three months, will prevent the recurrence of tinea pedis in a population with a verifiable history of recurrent disease (defined as: positive microscopy and/or culture on record from a prior episode of tinea pedis)

The purpose of the open label extension is to acquire additional longitudinal data on cutaneous fungal isolates during extended terbinafine therapy as well as to obtain additional efficacy and safety information regarding extended term use of prophylactic treatment

The purpose of the DNA testing will attempt to determine whether people with frequent tinea pedis have any common genetic patterns.

**Technical Approach:** This randomized, placebo-controlled, multi-dose, double-blind, multicenter study is designed to determine whether terbinafine HCl cream, 1%, when used once a day for seven consecutive days every three months, will prevent the recurrence of tinea pedis in a population with verifiable history of recurrent disease. 400 patients will be enrolled and randomly assigned to either the terbinafine arm of the study or the placebo arm. Both groups will apply their respective creams to their feet once a day for seven consecutive days every three months. The primary outcome of the study is the duration of prevention of tinea pedis.

**Progress:** This study was terminated by the sponsor 22 August 2000, due to FDA concerns about the study methods. No patients were enrolled in this study at MAMC prior to its termination.



## Detail Summary Sheets

Endocrinology Service,  
Department of Medicine



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/124

**Status:** Completed

**Title:** The Effect of Partial Energy Restriction on the Changes in Metabolic and Kinetic Measures of Thyroid Hormone Metabolism During Antarctic Residence

**Principal Investigator:** COL H. Lester Reed, MC

**Department:** Medicine/Endocrinology

**Facility:** MAMC

**Associate Investigator(s):** LTC Homer J. Lemar Jr., MC; MAJ Nhan V. Do, MC; Nancy S. Finney

**Start Date:**  
7/18/1997

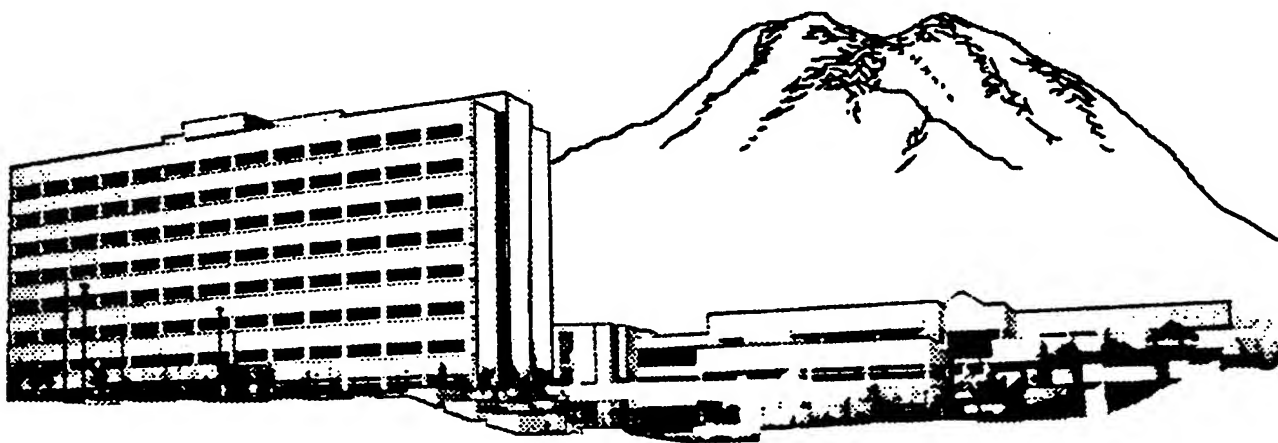
**Est. Completion Date:**  
Oct 98

**Periodic Review:**  
6/22/1999

**Study Objective:** 1) To evaluate the influence of circulating TSH and energy restriction upon the previously described increases in triiodothyronine (T3) plasma appearance rate and distribution volume (Vd) observed with extended Antarctic residence (AR). A reduction in serum TSH will be obtained by using 50mcg per day of thyroxine supplementation for the entire 11 month period, in contrast to our current study evaluating thyroxine supplement during the last 7 months of deployment. This dose schedule will allow an extension of our earlier findings regarding the effects of AR upon memory performance in this group. 2) To continue our previous mood and cognitive studies in the current study by contrasting placebo and thyroxine supplementation to insure the cognitive performance goal of supplementation has been achieved during the year as identified in our previous study.

**Technical Approach:** Sixteen military and civilian health care beneficiaries including men and women who are between 18 and 55 years old and are members of the winter-over crew in McMurdo, Antarctica will be recruited for the study. After recruitment subjects will perform monthly exercise, mood, and cognitive testing beginning one month prior to departure and continuing through their entire 11 month stay in McMurdo. The parameters that will be examined include changes in muscle oxygen utilization, changes in thyroid functions, and changes in cognitive, memory, and mood during the development of the Polar T3 Syndrome. One of the characteristics of the Polar T3 Syndrome is a low T4 state in the CNS that may be responsible for the characteristic declines in mood and memory during winter seasons in circumpolar regions. All subjects will receive either thyroxine 50mcg/day or daily placebo starting the day after October 1997 baseline studies and ending 11 months later in August 1998. Thyroid functions will be monitored monthly throughout the study. Subjects will serve as their own controls for analysis of kinetic parameters, mood and cognitive data. Comparisons will also be made between levothyroxine and placebo groups for the exercise, mood, cognitive testing, and kinetic parameters.

**Progress:** This study was reported as completed in FY99; however, at the request of COL Reed, the study was reactivated, 29 Dec 99, for the purpose of conducting additional serum assays on frozen stores serum collected during Antarctic studies. Assays were completed and the study was closed 31 May 00.



## Detail Summary Sheets

Gastroenterology Service,  
Department of Medicine

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/005

**Status:** Completed

**Title:** Intron A + Ribavirin for Treatment of Patients with Chronic Hepatitis C not Previously Treated with Interferon

**Principal Investigator:** MAJ William K. Hirota, MC

**Department:** Medicine/Gastroenterology

**Facility:** MAMC

**Associate Investigator(s):** COL Amy M. Tsuchida, MC; LTC Robert H. Sudduth, MC; LTC Spencer S. Root, MC

**Start Date:**  
10/17/1997

**Est. Completion Date:**  
Dec 98

**Periodic Review:**  
9/28/1999

**Study Objective:** To provide ribavirin for use in combination with Intron A for the treatment of Hepatitis C in patients who have not previously received interferon therapy; to obtain additional safety information of the combination on Intron A and ribavirin; to obtain additional information on different regimens of Intron A and ribavirin.

**Technical Approach:** Subjects will be randomized to either Intron A plus ribavirin or Intron A plus placebo. Treatment for the first 12 weeks will be double-blind. At 12 weeks, blood test for HCV-RNA will be done to assess response. If the test is positive, treatment will be unblinded and those on placebo will be offered to cross over to treatment with Intron A plus ribavirin. If they were on ribavirin, they will be finished with the study. If the test is negative, subjects will continue with their current blinded treatment.

**Progress:** This study was reported as completed at MAMC, 9 Jun 00, with nine subjects consented; 3 withdrew prior to drug administration, 2 withdrew secondary to adverse events and 4 completed study requirements. All subjects continue to be seen in the GI Clinic for regular follow-up.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/006	<b>Status:</b> Completed
<b>Title:</b> Intron A + Ribavirin for Treatment of Patients with Interferon-Refractory or Interferon-Relapsed Chronic Hepatitis C		
<b>Principal Investigator:</b> MAJ William K. Hirota, MC		
<b>Department:</b> Medicine/Gastroenterology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Amy M. Tsuchida, MC; LTC Robert H. Sudduth, MC; LTC Spencer S. Root, MC		
<b>Start Date:</b> 10/17/1997	<b>Est. Completion Date:</b> Dec 98	<b>Periodic Review:</b> 9/28/1999

**Study Objective:** To provide ribavirin for use in combination with Intron A for the treatment of Hepatitis C patients who failed previous interferon therapy or relapsed after treatment with interferon; to obtain additional safety information on the combination of Intron A and ribavirin; to obtain additional information on different regimens of Intron A and ribavirin.

**Technical Approach:** Patients will be treated throughout the study with open-label Intron A and ribavirin; dose dependent on weight. Safety and tolerance will be evaluated at weeks 1, 2, 4, 8, and then every 4 weeks during treatment and at weeks 4, 8, 12, and 24 until the end of therapy. Complete response will be defined as loss of detectable HCV-RNA by PCR.

**Progress:** This study was reported as completed at MAMC, 6 Jun 00, with four subjects consented, 3 withdrew secondary to adverse events and 1 patient completed all study requirements. All subjects continue to be seen in the GI clinic for regular follow-up.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/031

**Status:** Ongoing

**Title:** The Use of a Nutritional Supplement as an Antimicrobial in *Helicobacter pylori* Eradication

**Principal Investigator:** LTC Jonathan P. Kushner

**Department:** Medicine/Gastroenterology

**Facility:** MAMC

**Associate Investigator(s):** James R. Wright, M.T.; LTC Spencer S. Root, MC; MAJ William K. Hirota, MC; Janet C. Chilton

**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
N/A

**Study Objective:** To assess the antimicrobial action of garlic on *Helicobacter pylori*: to attempt to eradicate *Helicobacter pylori* with the combination of garlic and a proton-pump inhibitor in a double-blinded, placebo-controlled trial; also, to assess changes in symptoms, endoscopic appearance, histology, quantitative cultures, quantitative urease activity (by breath test) and serum and gastric tissue cytokines following the eradication attempt.

**Technical Approach:** After screening up to 500 candidates with *H. pylori* serology, as well as a standardized GI Likert (17) scale dyspepsia symptom questionnaire and a food frequency questionnaire, two 7 mL red top blood tubes (one for *H. pylori* serology and one for cytokine assays) and one complete blood count will be drawn at the time of the initial screening. Those with positive serology will be asked to discontinue PPI, and if possible, non-steroidal antiinflammatory medications. Active *H. pylori* infection will be confirmed in patients with positive serology by the presence of either positive *H. pylori* on histology and a positive rapid urease test. At endoscopy, after aspiration of gastric juice, seven biopsies will be obtained from the antrum, and seven from the body of the stomach. One biopsy from each will be used for the RUT test, with two for histology and two for *H. pylori* culture. The sixth biopsy will be frozen in liquid nitrogen for cytokine mRNA expression and the seventh biopsy, as well as the gastric aspirate, assayed for cytokine protein. Patients positive for *H. pylori* infection will be stratified into either a low/normal habitual garlic consumption. Patients will be blocks of 15 Those in the treatment blocks will receive three garlic supplement capsules twice daily while those in the placebo blocks will receive six identically appearing capsules. Patients will refrain from antibiotic, PPI, bismuth, and if possible, NSAID use during this period. Blood work and endoscopy will be repeated for purposes of research and data collection.

**Progress:** Ten patients have been enrolled in this study in FY00 at MAMC. Six have undergone endoscopy. Three patients have confirmed active *H. pylori* infection and are about to begin the randomized 4-week treatment trial. Four patients have endoscopy scheduled. No adverse events have been reported and subject enrollment continues.

### Detail Summary Sheet

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<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/144	<b>Status:</b> Ongoing
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**Title:** A Randomized, Double-blind, Placebo-controlled, Dose Finding, Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Tegaserod Given Orally at Three Dose Levels and Placebo in Patients with Functional Dyspepsia and Documented Delayed Gastric Emptying

**Principal Investigator:** COL Amy M. Tsuchida, MC

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**Department:** Medicine/Gastroenterology

**Facility:** MAMC

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**Associate Investigator(s):** MAJ Robert K. Durnford, MC; MAJ Eric J. Ormseth, MC; LTC Jonathan P. Kushner

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**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Oct 01

**Periodic Review:**  
N/A

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**Study Objective:** (1) To determine in patients with symptoms of dyspepsia and documented delay in gastric emptying rate the efficacy of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo as measured by satisfactory relief of meal related upper stomach problems and (2) to rate the effects of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo; (3) patient's assessment of symptoms of functional dyspepsia; (4) patient's quality of life and (5) the safety and tolerability.

**Technical Approach:** This is a multicenter, Phase II dose-finding trial with a parallel group design in patients with functional dyspepsia and delayed gastric emptying as measured by scintigraphy. Following a one week screening and a two week washout period, eligible subjects will be randomized to receive either placebo tid or daily doses of 1.5 mg, 6 mg or 18 mg Zelmec (tegaserod) given orally tid for 8 weeks. Data will be collected on patient symptoms of dyspepsia and quality of life. Drug compliance, concomitant medications and adverse events will be monitored.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/145

**Status:** Ongoing

**Title:** A Randomized, Double-blind, Placebo-controlled, Dose Finding, Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Tegaserod Given Orally at Three Dose Levels (1.5 mg, 6 mg, 18 mg) and Placebo in Patients with Functional Dyspepsia (FD) and Documented Normal Gastric Emptying

**Principal Investigator:** COL Amy M. Tsuchida, MC

**Department:** Medicine/Gastroenterology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert K. Durnford, MC; MAJ Eric J. Ormseth, MC; LTC Jonathan P. Kushner

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Oct 01

**Periodic Review:**  
N/A

**Study Objective:** (1) To determine in patients with symptoms of dyspepsia and documented normal gastric emptying rate the efficacy of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo as measured by satisfactory relief of meal related upper stomach problems and (2) to rate the effects of daily doses of 1.5, 6 and 18 mg of tegaserod, given orally tid versus placebo; (3) patient's assessment of symptoms of functional dyspepsia; (4) patient's quality of life and (5) the safety and tolerability.

**Technical Approach:** This is a multicenter, Phase II dose-finding trial with a parallel group design in patients with functional dyspepsia and normal gastric emptying as measured by scintigraphy. Following a one week screening and 2 week washout period, eligible subjects will be randomized to receive either placebo tid or daily doses of 1.5 mg, 6 mg or 18 mg Zelmec (tegaserod) given orally tid for 8 weeks. Data will be collected on patient symptoms of dyspepsia and quality of life, and drug compliance, concomitant medications and adverse events will be monitored.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 96/164	<b>Status:</b> Ongoing
<b>Title:</b> Epidemiology of Gallbladder Sludge and Stones in Pregnancy		
<b>Principal Investigator:</b> COL Amy M. Tsuchida, MC		
<b>Department:</b> Medicine/Gastroenterology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Sum P. Lee, M.D., Ph.D; MAJ Kazunori Yamamoto, MC; COL Roderick F. Hume, MC; LTC Byron C. Calhoun, MC, USAF; Scott J. Schulte, M.D.; Beth W. Alderman, M.D., MPH; Dr. Gerard Schellenberg, M.D.; Edward J. Boyko, M.D., Ph.D.; Gail Jarvik, M.D.; Katherine H. Moore, Ph.D.; MAJ Janice C. Stracener, MC; COL Dawn E. Light, MC		
<b>Start Date:</b> 9/20/1996	<b>Est. Completion Date:</b> Sep 02	<b>Periodic Review:</b> 9/26/2000

**Study Objective:** The primary objective of this NIH-funded study is to determine the incidence of gallstones and sludge during pregnancy. Other objectives are to: 1) identify behavioral and genetic risk factors for the development and regression of sludge and stones; 2) elucidate the mechanism by such risk factors may induce gallstones; and 3) predict the development and regression of sludge and stones.

**Technical Approach:** This cohort study will include serial ultrasound tests of the gallbladder during pregnancy and post-partum. All women presenting for prenatal care will be eligible unless they: (1) do not speak English; (2) have had gallbladder surgery; (3) are over 20 weeks pregnant; (4) do not expect to deliver at MAMC; and (5) are less than 18 years of age. Eligible women who agree to participate will complete Participation and Consent Forms and under waist and hip circumference measurements. the ultrasonographers will test participants for evidence of sludge and stones at 10, 18, and 28 weeks of gestation and 6 weeks postpartum. For each ultrasound test, the study radiologist will review selected ultrasound images saved by the ultrasonographer. Participants who have stones or sludge at 6 weeks postpartum will return in 12 year for a follow-up ultrasound. At her time of each ultrasound, participants will be asked to complete a one-hour questionnaire and interview. They will also be asked to give an extra fasting blood sample at 128 weeks of gestation. Medical data from the CIS and CHCS will be downloaded and linked to study data.

**Progress:** 1,227 subjects have been enrolled in this study during FY 00, for a total of 4488 subjects. To date, 1842 subjects have completed the study. 1362 subjects were lost to follow-up due to PCS/ETS, miscarriage and non-compliance. 1284 subjects are still in some phase of the study. 20 subjects have had gall bladder surgery and 70 subjects have been referred to the gastroenterology clinic for further follow-up. Subject recruitment is ongoing.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/012	<b>Status:</b> Ongoing
<b>Title:</b> A Pre-Clinical Research and Development Study to Evaluate Stool Specimens for Basement Membrane Fragments/Complexes and Cytoskeletal Proteins		
<b>Principal Investigator:</b> COL Amy M. Tsuchida, MC		
<b>Department:</b> Medicine/Gastroenterology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Robert H. Sudduth, MC; MAJ Kazunori Yamamoto, MC; MAJ John G. Carrougner, MC		
<b>Start Date:</b> 11/15/1996	<b>Est. Completion Date:</b> Oct 97	<b>Periodic Review:</b> 10/24/2000

**Study Objective:** Evaluate the clinical utility potential of the CoTA test strip assay in detecting basement membrane complexes in individuals with or without colorectal cancer, respectively. And to isolate sufficient amounts of colon BMC for additional antibody production and antigen characterization using the CoTA test strip assay and other antibody tests.

**Technical Approach:** This is a multicenter trial with MAMC providing stool specimens only from patients diagnosed with colorectal cancer. Following colonoscopy, eligible participants will be instructed to collect a stool specimen after their stools have returned to normal and prior to any other intestinal procedures. The specimen will be shipped directly to BARD Diagnostic Sciences, Inc.

**Progress:** 74 subjects have been enrolled in this study at MAMC and completed study requirement. 53 subjects enrolled in this study in FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/004

**Status:** Ongoing

**Title:** Epidemiology of Barrett's Esophagus

**Principal Investigator:** COL Amy M. Tsuchida, MC

**Department:** Medicine/Gastroenterology

**Facility:** MAMC

**Associate Investigator(s):** Diana C. Farrow, Ph.D.; MAJ William K. Hirota, MC; LTC Spencer S. Root, MC; LTC Robert H. Sudduth, MC

**Start Date:**  
10/17/1997

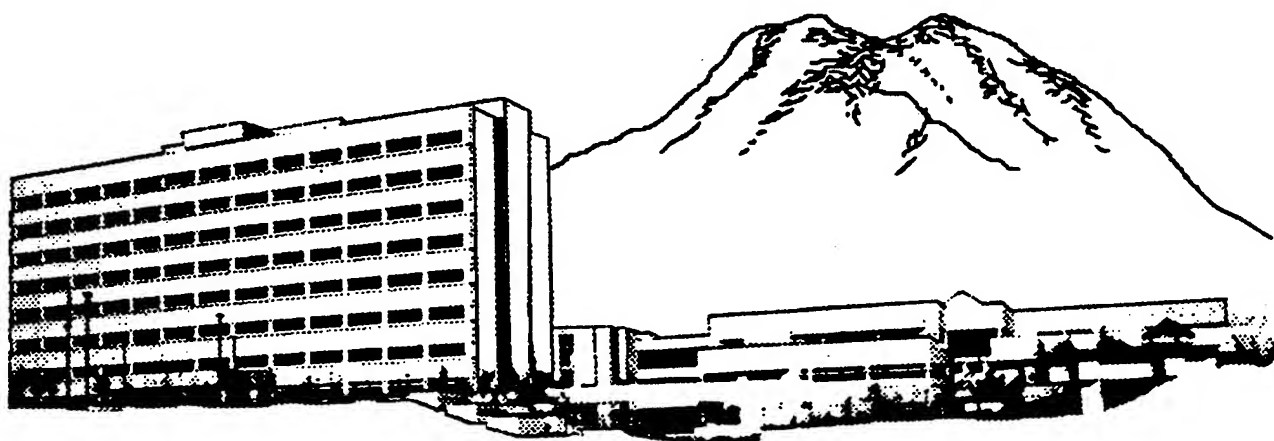
**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
10/24/2000

**Study Objective:** To determine whether there are any specific environmental, dietary, or personal factors which increase the risk of developing Barrett's Esophagus.

**Technical Approach:** Patients who are undergoing an upper endoscopy for evaluation of their heartburn complaints will have four biopsies and a small amount of stomach fluid taken for research purposes. Information from the endoscopic findings will be abstracted from medical records.

**Progress:** 90 subjects have been enrolled in this protocol. Of the 11 subjects recruited during FY00, 2 were diagnosed with Barrett's; a total of 6 patients were recruited for interviews. While statistical analyses are underway, it is too early for findings.



## Detail Summary Sheets

Hematology/Oncology Service,  
Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/011	<b>Status:</b> Terminated
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**Title:** A Randomized, Double-blind, Placebo-Controlled, Parallel-Group, Dose-Finding Study, Conducted Under In-House Blinding Conditions, to Examine the Safety, Tolerability, and Efficacy of MK-0869 for the Prevention of Chemotherapy-Induced Emesis Associated with Moderately Emetogenic Chemotherapy

**Principal Investigator:** MAJ David E. McCune, MC

<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Ines J. Sanchez-Rivera, MC; MAJ Matthew P. Jones, MC; Shirley Newcomb, BSN, MPH

**Start Date:**  
10/26/1999

**Est. Completion Date:**  
May 00

**Periodic Review:**  
N/A

**Study Objective:** To compare MK-0869 triple therapy (high dose) with standard therapy in the control of delayed CIE as measured by the proportion of patients with Total Control on Days 2 to 5 and to evaluate the safety and tolerance of triple therapy with MK-0869 (both dose regimens).

**Technical Approach:** Patients will be randomly assigned to 1 of 3 treatment groups. All 3 treatment groups will receive dexamethasone and ondansetron orally on Day 1 followed by ondansetron orally on Day 2. Patients in Group I (high dose triple therapy) will also receive MK-0869, 375 mg, on Day 1, followed by 250 mg on Days 2 to 5. Patients in Group II (low dose therapy) will also receive MK-0869, 125 mg, on Day 1, followed by 80 mg on Days 2 to 5. Patients in Group III (standard therapy) will receive MK-0869 placebo on Days 1 to 5. Patients will be instructed to take "rescue therapy" if needed for nausea or emesis. Emetic events or rescue therapy will be recorded by the patient in a diary from the initiation of chemotherapy infusion (Day 1) until the morning of Day 6.

**Progress:** This protocol was terminated by the sponsor, 5 Jun 00, before it could be implemented at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/020	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Double-Blind, Placebo-controlled, Parallel-Group, Dose-Finding Study, Conducted Under In-House Blinding Conditions, to Examine the Safety, Tolerability, and Efficacy of MK-0869 for the Prevention of Acute Delayed Chemotherapy-Induced Emesis Associated with High-Dose Cisplatin		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC; MAJ Matthew P. Jones, MC		
<b>Start Date:</b> 11/19/1999	<b>Est. Completion Date:</b> May 00	<b>Periodic Review:</b> N/A

**Study Objective:** This study will (1) compare MK-0869 triple therapy (high dose) with standard therapy in the control of delayed CIE as measured by the proportion of patients with a Complete Response on Days 2-5, (2) compare MK-0869 triple therapy (high dose) with standard therapy in the control of acute CIE as measured by the proportion of patients with a Complete Response on Day 1 and (3) compare the tolerability of triple therapy with MK-0869 (both doses) relative to standard dual therapy in cancer patients receiving high-dose cisplatin.

**Technical Approach:** Eligible subjects will have their medical history taken and a physical examination. On the same day of cyclophosphamide treatment (Day 1), subjects will receive oral ondansetron 8 mg twice daily and an oral dose of dexamethasone 20 mg. Subjects will receive either oral MK-0869 375 mg once daily, or oral MK-0869 125 mg once daily, or placebo. On the day after cyclophosphamide treatment (Day 2), subjects will receive oral doses of ondansetron 8 mg twice daily and either oral MK-0869 250 mg once daily or oral MK-0869 80 mg once daily or placebo. The following 3 days (Days 3-5) after chemotherapy, subjects will receive either oral MK-0869 250 mg once daily or oral MK-0869 80 mg once daily or placebo.

Subjects will be required to visit the study doctor 4 times during each chemotherapy cycle. At each visit subjects will have vital signs taken, an ECG, blood drawn (in the first cycle and following cycles), complete a diary card to show vomiting or dry heaves and how much nausea experienced over 24 hours, and any rescue medications used.

**Progress:** One patient was enrolled in FY00 and continues to be followed. The protocol was recently closed to patient enrollment per the sponsor.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/057	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Double-blind, Placebo Controlled Trial of Gemcitabine plus Placebo versus Gemcitabine plus R115777 in Patients with Advanced Pancreatic Cancer		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC; MAJ Matthew P. Jones, MC		
<b>Start Date:</b> 3/28/2000	<b>Est. Completion Date:</b> Dec 05	<b>Periodic Review:</b> N/A

**Study Objective:** (1) This study will determine whether the addition of R115777 to standard gemcitabine therapy improves overall median survival time by 36% in comparison to gemcitabine plus placebo, (2) compare quality of life (QOL) between the two arms, (3) compare the objective response rate, progression free survival and duration of objective response, (4) estimate 6 month and one-year survival rates of the two arms, (5) assess the safety of the two arms based on laboratory and clinical parameters, and (6) determine the incidence of ras mutations in patients with tissue blocks available for analysis.

**Technical Approach:** This is a randomized, double-blind, placebo controlled Phase III study for patients with pancreatic cancer. All participating patients will receive gemcitabine and be randomized to R115777 versus placebo. Gemcitabine, 1000 mg/m<sup>2</sup> will be administered intravenously weekly for 7 consecutive weeks followed by one week of rest. The study drug, R115777, or placebo will be given orally, 2 dosage units, twice daily, continuously. Treatment will be given until progression or the development of unacceptable toxicity. All patients will be followed indefinitely.

**Progress:** No patients were enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/085

**Status:** Ongoing

**Title:** A Phase II Trial of Recombinant-Human Granulocyte-Macrophage Colony Stimulating Factor (rhu-GM-CSF, Leukine) in Chronic Diabetic and Venous Stasis Wounds

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** Medicine/Hematology & Oncology

**Facility:** MAMC

**Associate Investigator(s):** Vickie R. Driver, MS, DPM

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
N/A

**Study Objective:** (1) Assess the efficacy of applying rhu-GM-CSF peri-lesionally to chronic diabetic and venous chronic wounds at a dose of 500mcg twice weekly to decrease time to wound healing and (2) Assess the safety, as an adjunct to standard wound care, of peri-lesional rhu-GM-CSF to improve time to wound healing.

**Technical Approach:** This study is an open, single-arm pilot study. 30 male/female eligible patients, over 18 years-old, with chronic wounds as a result of the verifiable diagnosis of diabetes or venous stasis will receive rhu-GM-CSF (Leukine) twice weekly through peri-lesional injection in a four-points-of-the-compass fashion of their wounds for a total of twenty weeks. Wound size will be measured at entry, at each visit, and at the conclusion of therapy. The change in the cross-sectional area of the wound will be recorded for each patient and reported as the primary endpoint of the study. Patients will be sequentially enrolled with interim analysis at twenty patients. The secondary endpoint of the study is the incidence of toxicity with the study drug. Toxicity will be assessed at every visit, and recorded according to the NCI Common Toxicity Criteria. Efficacy will be measured by comparison to historical records and safety monitored throughout the study. This data will be used to initiate a phase III trial to develop and utilize a topical gel formulation of rhu-GM-CSF.

**Progress:** This protocol has not yet received final IRB approval.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/086	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Study of Herceptin, Taxol, and Paraplatin in Hormone Refractory Prostate Cancer that Overexpresses HER2-neu		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 5/23/2000	<b>Est. Completion Date:</b> Jan 02	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To determine the response rate in HRPC to weekly administration of Herceptin, paclitaxel and Carboplatin. Response rate is defined as the percentage of enrolled patients who achieve a best response of complete or partial response. Rates of complete response, partial response, stable disease and progressive disease will be reported, (2) To assess the relative toxicity of adding Herceptin to the chemotherapy regimen.

**Technical Approach:** This is a Phase II, multicenter trial with a primary outcome variable of response rate to weekly administration of Herceptin, paclitaxel and carboplatin. Subjects with hormone refractory prostate cancer (HRPC) will be eligible for entry into the study. All subjects will have tissue biopsy of a metastatic site. That site will be analyzed for HER2 over expression. Patients with HRPC who over express HER2 will be treated with weekly Herceptin, paclitaxel and carboplatin and followed for response. Other endpoints will be median survival, median time to progression, and the rate of toxicity to this treatment.

**Progress:** This protocol has not yet received final IRB approval.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/097	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-blind, Phase III Comparative Trial of 2 Doses of ZD1839 (IRESSA) in Combination with Gemcitabine and Cisplatin Versus Placebo in Combination with Gemcitabine and Cisplatin in Chemotherapy Naive Patients with Advanced (Stage III or IV) Non-small Cell Lung Cancer, Protocol 1839IL/0014 COV-1935		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC; LTC James J. King, MC; LTC David T. Schachter, MC; LTC Michael J. Wilson, MC; COL Kevin J. Chismire, MC		
<b>Start Date:</b> 6/27/2000	<b>Est. Completion Date:</b> Jun 02	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To demonstrate an increase of 35% in the 1-year survival rate for ZD1839 compared to placebo, (2) To demonstrate a statistically significant improvement in time to worsening of disease-related symptoms based on the FACT-L lung cancer subscale (LCS) for ZD1839 compared to placebo, (3) to demonstrate a statistically significant improvement in progression free survival for ZD1839 compared to placebo, (4) to demonstrate a higher symptom improvement rate based on the FACT-L LCS for ZD1839 compared to placebo, (5) to demonstrate an improvement in the overall objective response rate (complete + partial response) for ZD1839 compared to placebo, (6) to provide an estimate of the duration of response (complete + partial response) for each treatment arm, (7) to demonstrate an improvement in the disease control rate (complete + partial response) for ZD1839 compared to placebo, (8) to demonstrate a quality of life for ZD1839-treated patients that is as good as or better than that for placebo-treated patients, (9) to establish a manageable safety profile of ZD1839 in combination with chemotherapy that is compatible with chronic use, (10) to assess the correlation of Epidermal Growth Factor Receptor (EGFR) expression with survival, adjusted for dose and baseline chemotherapy, using data from trials 1839IL/0017 and 1839IL/0014, (11) to compare the adverse event profile and survival of 2 doses of ZD1839 given with and following chemotherapy and (12) to investigate the demographic and pathophysiological factors of patients affecting exposure to ZD1839.

**Technical Approach:** This is a randomized, parallel-group, double-blind, placebo-controlled, multicenter trial. All chemotherapy naive patients with non-small cell lung cancer (NSCLC) Stage III or IV will receive standard of care (gemcitabine and cisplatin), and will be randomized to one of the following three treatment groups; (1) ZD 1839, 250 mg/day, (2) ZD 1839, 500 mg/day or (3) placebo. Subjects will be further stratified by weight loss in previous 6 months, disease State III versus disease Stage IV, performance status 0-1 versus 2 and measurable disease versus non-measurable disease. The medication will be taken twice (about 12 hours apart) on Day 1 to assure rapid achievement of steady state levels. The study drug will be taken once a day from Day 2 onwards. All subjects will receive gemcitabine, IV, 1000 mg/m<sup>2</sup> on days 1, 8, and 15 and cisplatin IV, 100 mg/m<sup>2</sup> on days on Day 1 only with 3 liters of fluids. The chemotherapy cycles will be repeated every 4 weeks for a maximum of 6 cycles.

Study drug or matching placebo will be taken daily until disease progression, or 6 months after the last subject has been recruited. Upon closure and breaching of the blind for the trial, subjects continuing to show evidence of response or clinical benefit from the study drug may continue to receive ZD 1839 under a separate protocol.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/114	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Multicenter, Randomized, Active-controlled Clinical Trial to Evaluate the Efficacy and Safety of rhuMab-VEGF (BEVACIZUMAB) in Combination with Standard Chemotherapy in Subjects with Metastatic Colorectal Cancer (AVF2107g)		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 7/25/2000	<b>Est. Completion Date:</b> Sep 04	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the efficacy of multiple administrations of rhuMab-VEGF (5mg/kg every 2 weeks) when combined with chemotherapy versus 5-FU/leucovorin/CP-11 for treatment of metastatic colorectal cancer, as measured by duration of survival and to evaluate the safety of multiple administrations of rhuMab-VEGF (5mg/kg every 2 weeks) when combined with chemotherapy versus 5-FU/leucovorin/CP-11 for treatment of metastatic colorectal cancer.

**Technical Approach:** rhuMab-VEGF (Bevacizumab) is an experimental, humanized monoclonal antibody using recombinant DNA technology, directed against vascular endothelial growth factor, or VEGF. Following a 28 day screening period, eligible subjects will be randomized into one of three treatment arms, (1) 5-FU/leucovorin/CPT-11 plus placebo, (2) 5-FU/leucovorin/CPT-11 plus study drug, or (3) 5-FU/leucovorin plus study drug. The treatment period will last approximately 23 months with a 14 day follow-up. Subjects will be asked to periodically complete Quality of Life Questionnaires and blood samples will be sent to an outside lab for pharmacokinetic testing. Second-line treatment options will be offered under this protocol if there is disease progression, depending on the treatment arm originally assigned. Subjects will be removed from the study if the disease progresses further following second-line treatment. A safety analysis will be conducted after the first 50 patients treated with the study drug and CPT-11. At the conclusion of the study, if the tumor is stable or smaller and if subjects received rhuMab-VEGF, they may be eligible to continue to receive the study drug under an extension study.

**Progress:** No patients have been enrolled on this newly approved protocol. Patient screening has begun.

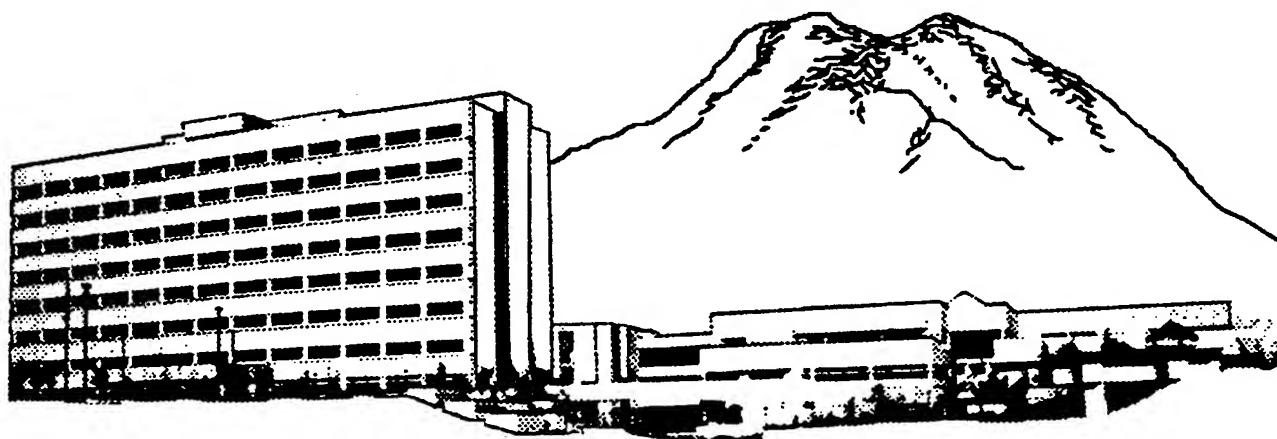
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/093	<b>Status:</b> Ongoing
<b>Title:</b> Phase II Trial of Gemcitabine and Herceptin in HER2 Overexpressing Metastatic Breast Cancer		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Jul 01	<b>Periodic Review:</b> N/A

**Study Objective:** 1) To response rates of complete response, partial response, stable disease and progressive disease. 2) To document the median time to progression and median survival of disease. 3) To monitor toxicities of Grades 3 or higher to be reported (toxicities graded based on the NCI common toxicity grading scheme).

**Technical Approach:** This is a Phase II multicenter trial conducted in military medical centers experienced in the treatment of breast cancer. The study will investigate the response rate, time to treatment failure, overall survival and toxicity/safety profile of a novel combination of Gemcitabine and Herceptin in patients with metastatic breast cancer. Both of the drugs will be administered weekly in patients whose breast cancer overexpresses the BER2 proto-oncogene.

**Progress:** This protocol has not yet received final IRB approval.



## **Detail Summary Sheets**

Infectious Disease Service,  
Department of Medicine

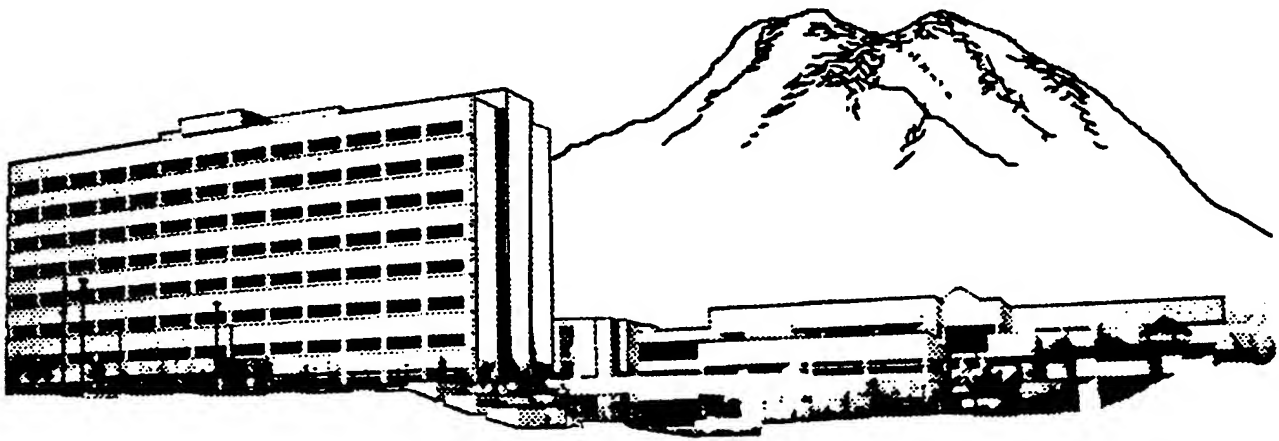
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/122	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Randomized, Double-blind Controlled Study to Evaluate the Safety and Immunogenicity of MEDI-516 with MF59C.1, an E. Coli Pilus Vaccine, in Adult Women at Risk for Recurrent Urinary Tract Infections		
<b>Principal Investigator:</b> LTC Joseph T. Morris III, MC		
<b>Department:</b> Medicine/Infectious Disease		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Kristie Lowry		
<b>Start Date:</b> 8/22/2000	<b>Est. Completion Date:</b> Nov 02	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to describe the safety and reactogenicity (serum and urine antibody responses) of three doses of MEDI-516 formulated in MF59C.1 in healthy adult women with a history of recurrent urinary tract infection (UTI). Describe and analyze the occurrence of UTIs in volunteers receiving at least one dose of vaccine.

**Technical Approach:** This randomized, double-blind, controlled Phase II study is designed to gather additional safety and immunogenicity data in healthy, sexually active female volunteers age 18-45 who have experienced symptomatic urinary tract infections (UTI) within the preceding 12 months. Volunteers will be monitored to describe local and general safety, reactogenicity, and immunogenicity of three doses of either 25 micrograms of MEDI-516 with MF59C.1 or adjuvant control administered on study days 0, 28, and 180. This study will also describe the occurrence of symptomatic UTI and asymptomatic bacteriuria caused by E. coli and other uropathogens, as these events are important in defining clinical endpoints that are critical to the design of Phase III Efficacy studies.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.



## Detail Summary Sheets

Internal Medicine Service,  
Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/032	<b>Status:</b> Ongoing
<b>Title:</b> Cost Analysis of Prescreening for Hepatitis A Before Immunization in Patients with Chronic Liver Disease		
<b>Principal Investigator:</b> CPT Marten B. Duncan, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ William K. Hirota, MC; COL Amy M. Tsuchida, MC; LTC Spencer S. Root, MC		
<b>Start Date:</b> 2/23/1999	<b>Est. Completion Date:</b> Feb 01	<b>Periodic Review:</b> 3/28/2000

**Study Objective:** To define the prevalence of hepatitis A virus (HAV) in a population of patients with chronic liver disease (CLD) and to characterize demographic features of previously exposed patients. To perform a cost analysis of immunization for hepatitis a virus in those with CLD by comparing three strategies.

**Technical Approach:** 100 subjects with CLD will be recruited to clarify the prevalence of prior hepatitis A exposure. Subjects will complete a survey to identify which risk factors are most common among patients with CLD. Hepatitis A serology will then be determined using an anti-HAV elisa. Subjects will be asked to report for vaccination only if they are seronegative for prior exposure to the virus. A cost analysis will be done to identify the least costly way to provide immunity against the virus in this subgroup of patients using the prevalence of prior infection determined by this study. These strategies include: (1) to determine seropositivity and vaccinate only those without evidence of prior exposure, (2) to immunize all persons with CLD, or (3) determine antibody status and vaccinate in one visit with follow-up vaccination at 6 months only if the patient was seronegative for anti-HAV.

**Progress:** Data continues to be collected on 100 patients. After enrollment, patients underwent serologic evaluation for the hepatitis A antibody. Patients without prior infection were sent for the hepatitis A vaccination.

Since the study was initially authored, additional questions have been raised as to the immunogenicity of this vaccination in patients with chronic liver diseases. It is not clear whether this group should have a post vaccination serology after completion of the series to ensure seroconversion has taken place. This study remains ongoing and has been amended to accomplish follow-up serology on 47 patients.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 200/054	Status: Completed
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**Title:** Evaluation of Perceived Versus Actual Medication Regimens in Internal Medicine Patients

**Principal Investigator:** CPT Brian T. McKinley, MC

**Department:** Medicine/Internal Medicine

**Facility:** MAMC

**Associate Investigator(s):** CPT Brian P. Mulhall, MC; Matthew R. Rutledge, R.Ph.

**Start Date:**  
3/28/1999

**Est. Completion Date:**  
2000

**Periodic Review:**  
N/A

**Study Objective:** (1) To simultaneously evaluate and correlate the accuracy of a patient's prescription medical regimen as determined through a patient-completed questionnaire, nursing interview, and primary care provider interview and evaluation, (2) evaluate mechanisms by which patients remember their current medication (to include patient or provider derived lists, memory, caregivers, or discharge summaries) and variables which may influence their ability to remember their medication regimens.

**Technical Approach:** Patients presenting to the Adult Primary Care Clinic will be enrolled in the study over the course of two consecutive clinic days. Prior to being seen by the nurse or primary care provider, the patient will complete a questionnaire in the waiting area. After completion of the questionnaire, the patient will be seen by a nursing staff-member that will catalogue the prescription medication regimen. The method of collection for this data will be left to the discretion of the nurse and may include any or all of the following sources: patient or family member recall, patient list, computer evaluation of the medications through CHCS, review of medication bottles if available or chart review. This information will be reported on a form that the primary care provider will not thereafter be able to access. The primary care provider will then independently obtain the patient's prescription medication regimen with access to the same sources as the nursing staff. At the end of the office visit, the patient will be given a form with instructions to transcribe the actual medication regimen based on the prescription medication bottles they have at home. The patient will be asked to not report medication additions, deletions, or changes that have been made on the associated doctor visit. Patients not responding within one week will be contacted by phone and asked to complete the form via telephone interview. The authors of this protocol (researchers) will not have access to the previously collected information as we collect/transcribe mail-in questionnaire data.

**Progress:** 213 subjects were enrolled during FY00. Nurses and primary care providers were more accurate at reporting the patient's actual medication names and doses when compared with the patient questionnaires. With respect to primary care providers, accuracy at naming medications decreased as the number of medications increased with a low of 71.4% at 7 medications. Patients who reported their spouses as their medication managers were only able to name 65% of their medications correctly compared with 83% for those patients who reported managing their own medications

There is significant difference between perceived versus actual medication regimens which may be clinically relevant.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/015

**Status:** Terminated

**Title:** Use of Blood Cultures in the Evaluation of Febrile Episodes in Neutropenic Patients Receiving Broad Spectrum Antibiotics

**Principal Investigator:** CPT Brian P. Mulhall, MC

**Department:** Medicine/Internal Medicine

**Facility:** MAMC

**Associate Investigator(s):** COL Ronald H. Cooper, MC; MAJ Robert B. Gibbons, MC; CPT Sue E. Fitzgerald, MC

**Start Date:**  
11/21/1997

**Est. Completion Date:**  
Jul 98

**Periodic Review:**  
1/26/1999

**Study Objective:** To determine the prevalence of positive blood cultures in febrile granulocytopenic patients who are receiving antimicrobial therapy; whether blood culture results were used to modify antimicrobial therapy; the cost of obtaining blood cultures during these episodes and to determine, if possible, a population of patients in whom blood cultures are likely to be positive.

**Technical Approach:** The charts of febrile neutropenic patients admitted to MAMC from 1989 to 1997 will be reviewed with particular attention to blood culture results and antibiotic use. The cost of these blood cultures will be estimated. Data extracted will include: demographics, diagnoses, antibiotic use, chemotherapeutic regimen currently in use, daily ANC, blood cultures and clinical data.

**Progress:** No patients were enrolled in this study in FY 00 due to time limitations of the investigators. Due to the PCS of the principal investigator, this protocol was terminated by the IRB when a new PI could not be found to take over this project.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/066      **Status:** Completed

**Title:** Spot Uric Acid/Creatinine Ratio vs. 24 Hour Collection for Evaluation of Uric Acid Excretion

**Principal Investigator:** CPT Naomi R. Sullivan, MC

**Department:** Medicine/Internal Medicine

**Facility:** MAMC

**Associate Investigator(s):** MAJ David R. Finger, MC;

**Start Date:**  
4/27/1999

**Est. Completion Date:**  
Sep 99

**Periodic Review:**  
N/A

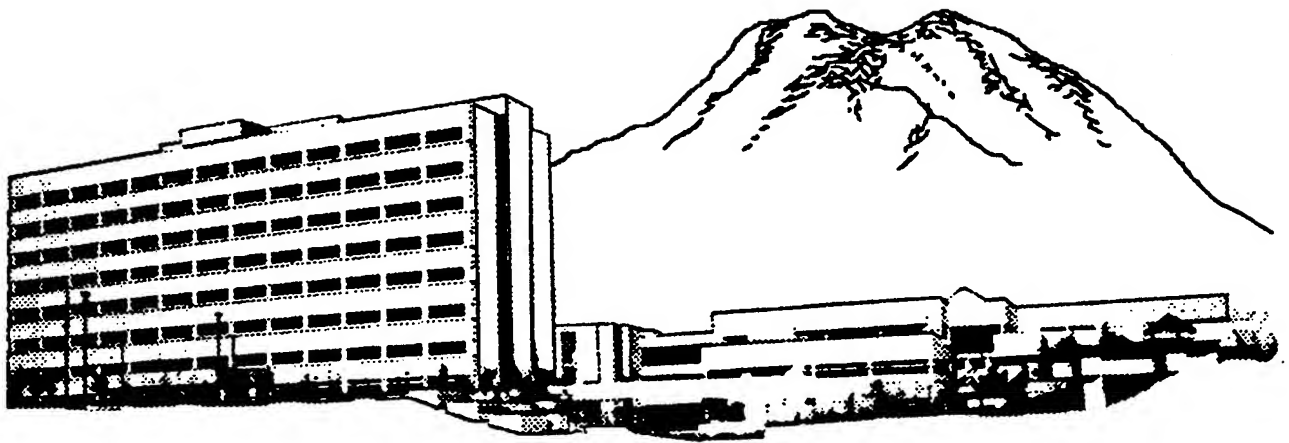
**Study Objective:** To determine if one time urine uric acid ratios strongly correlate with 24 hour urine collects in patients serving as their own controls.

**Technical Approach:** We are conducting a study of approximately 60 gout patients, 40 renal patients and 40 controls recruited from the Rheumatology, Nephrology and APC clinics to determine if one-time fractional excretion of uric acid is an accurate predictor of 24 hour uric acid excretion. Patients will be identified for the study by data abstraction from CHCS. Patients will be asked to perform a one-time serum and urine collection followed shortly by a 24 hour urine collection.

If they are willing to participate, a short history to determine age, sex, race, tobacco and alcohol use, diet, renal insufficiency, hyperlipidemia. Serum will be analyzed for creatinine and uric acid. Spot urine will be sent for uric acid and creatinine. A 24 hour urine sample will be analyzed for uric acid levels. Data collected will be made part of a permanent medical record.

Our hypothesis is that fractional excretion of uric acid will accurately predict 24 hour urinary acid excretor status (high or low). Primary analysis will be for correlation of three ratios with 24 hour uric acid measurements: urinary uric acid/creatinine ratio, fractional excretion of uric acid ( $\text{UA}(\text{serum}) \times \text{creatinine}(\text{urine}) / \text{uric acid}(\text{urine}) \times \text{creatinine}(\text{serum})$ ), and uric acid (urine x creatinine (serum)/uric acid (serum) ratio. Secondary analysis will be performed for factors that may interfere with this correlation (i.e. chronic renal insufficiency, high triglycerides). This analysis may identify a limited population in which spot urine/ serum measurements might suffice rather than 24 hour collections.

**Progress:** Thirty-two patients were enrolled with gout, diagnosed by either joint aspirate or meeting ACR criteria. Spot urine uric acid was compared to creatinine ratios, uric acid to creatinine clearance ratios, uric acid to creatinine clearance ratios and fractional excretion of uric acid to 24-hour uric acid measurements. Also examined were 21 normal controls. Results: Among the normal controls there was no correlation between the 24 hour collection and any of the three spot ratios. In the hyperuricemic gout patient group there was no correlation between the urine uric acid/creatinine clearance ratio or the fractional excretion of uric acid. However, the use of the uric acid/creatinine ratio demonstrated a statistically significant correlation in hyperuricemic gout patients. Conclusions: A spot urine acid/creatinine ratio may be useful in hyperuricemic gout patients. A spot urine uric acid/creatinine ratio may correspond to overexcretion of uric acid or >800 mg/day, A ratio of <.3 may correspond to underexcretion or <300 mg/day.



## **Detail Summary Sheets**

Nephrology Service,  
Department of Medicine

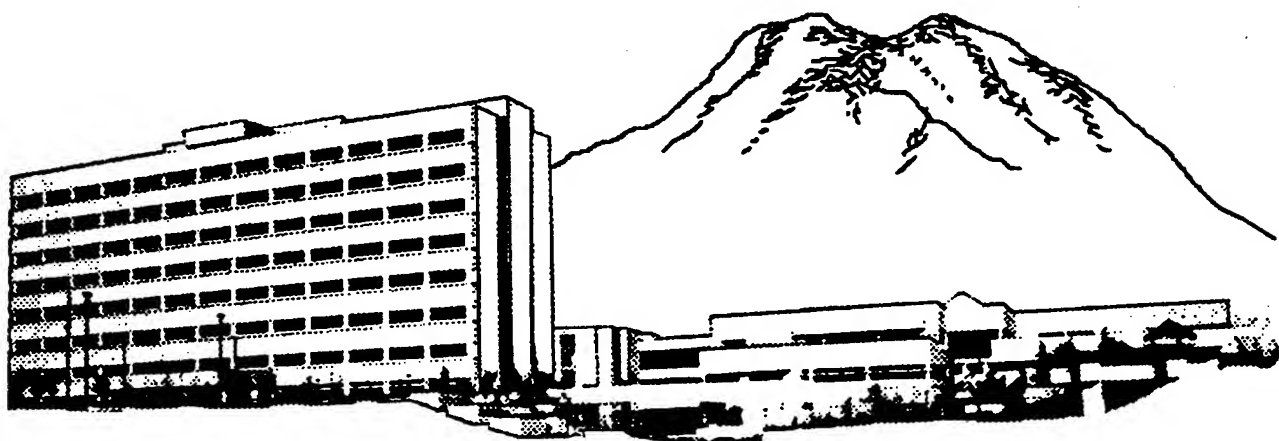
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/061	<b>Status:</b> Ongoing
<b>Title:</b> A Study Evaluating the Initiation and Titration of Fixed Doses of Novel Erythropoiesis Stimulation Protein (NESP) Therapy in Subjects with Chronic Renal Insufficiency			
<b>Principal Investigator:</b> MAJ Christopher J. LeBrun, MC			
<b>Department:</b> Medicine/Nephrology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.			
<b>Start Date:</b> 4/25/2000	<b>Est. Completion Date:</b> May 01		<b>Periodic Review:</b> N/A

**Study Objective:** To assess the use of NESP, when initiated and titrated as a fixed dose, necessary to achieve and maintain the hemoglobin (Hb) concentration within a target range (11.0 to 13.0 g/dL) in subjects with chronic renal insufficiency (CRI) and the safety and tolerability of chronic NESP therapy in subjects with CRI.

**Technical Approach:** This is a multicenter, open-label study designed to assess the use of NESP, when initiated and titrated as a fixed dose, necessary to achieve and maintain Hb with a target range (11.0 to 13.0 g/dL) in subjects with chronic renal insufficiency (CRI). The duration of the study for an individual patient is 27 weeks. After an initial 2-week screening/baseline period and 1-week baseline period during which time additional laboratory assessments will be performed, eligible subjects with CRI will initiate therapy with NESP. The initial dose of NESP will be based on the subjects' body weight. Each subject will receive a SC injection of NESP once weekly for a period of 24 weeks. The study concludes with a 1-week post treatment observation and evaluation period.

**Progress:** This recently approved protocol has not yet enrolled patients. Patient screening has begun.



## **Detail Summary Sheets**

Neurology Service,  
Department of Medicine

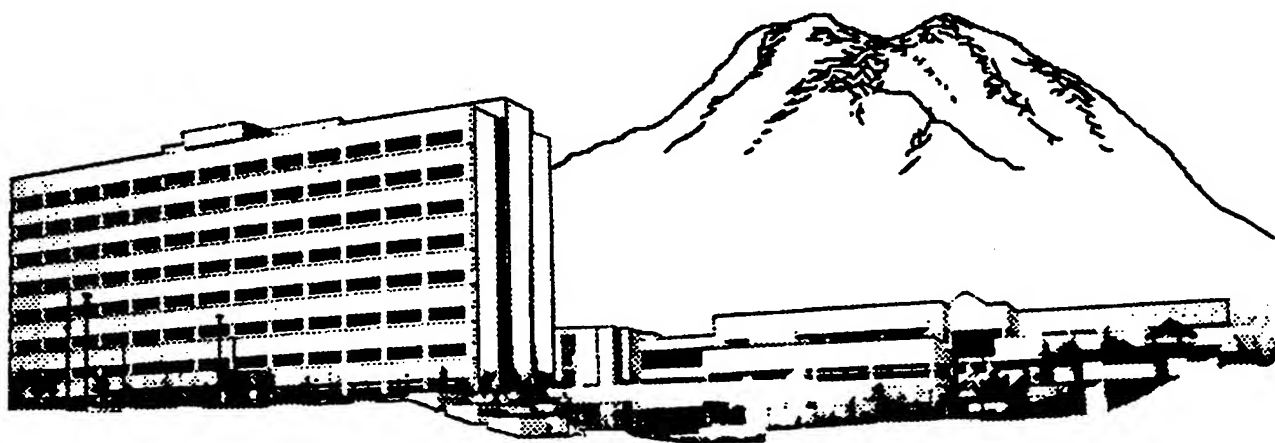
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/123	<b>Status:</b> Ongoing
<b>Title:</b> Carpal Tunnel Syndrome in Pregnancy: A Prospective Study on its Natural History		
<b>Principal Investigator:</b> MAJ John Hartmann, MC		
<b>Department:</b> Medicine/Neurology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Wendy Ma, MC; CPT Paul J. Walting, MC; CPT Anna M. Hohler, MC; COL Giorgio S. Turella, MC; LTC Beverly R. Scott, MC; MAJ Traci D. Ryan, MC; CPT Trenton James, MC		
<b>Start Date:</b> 8/22/2000	<b>Est. Completion Date:</b> Sep 02	<b>Periodic Review:</b> N/A

**Study Objective:** This study will try to determine the incidence of Carpal Tunnel Syndrome (CTS) during pregnancy in a prospective manner. Secondary objectives of this study will try to determine: (1) the incidence of CTS in each trimester of pregnancy; (2) potential risk factors for developing CTS in pregnancy such as Gestational Diabetes, preeclampsia, CTS in prior pregnancies, history of CTS prior to current pregnancy, excessive weight gain during pregnancy, nulliparous vs. multiparous pregnancies, single vs. multigestation pregnancies, concurrent hypothyroidism, and particular occupations; (3) the persistence of signs and symptoms of CTS after delivery and (4) pilot test a survey assessing Restless Leg Syndrome in pregnant women.

**Technical Approach:** This protocol will survey women seen in the Obstetric Clinic at MAMC for the development of CTS during each trimester and postpartum. Women will be enrolled at their first antepartum check and given a biographical sheet and questionnaire to complete, and an initial physical exam for the evaluation of CTS administered. The examiner will test the patient's ability to feel light touch, pinprick and 2 point discrimination at the points outlined. The examiner will then test muscle strength in the Abductor Pollicis Brevis, Opponens, Adductor Digiti Minimi, and Extensor Indicis Proprius. A Tinel's sign will be tested at each wrist, and Phalen's sign will be positive if sensory changes are reproduced in a median nerve distribution within 20 seconds of wrist flexion. At each evaluation, the presence of possible, probable, or definite CTS will be determined. Possible CTS will be defined as follows: Sensory changes to the hand, with nocturnal symptoms. Probable CTS will be defined as follows: Sensory changes with the hand, with nocturnal symptoms. Localization by physical exam would be defined as consistent sensory findings over areas supplied by branches of the median nerve traversing through the carpal tunnel (via pinprick and light touch). Definite CTS will be defined as follows: Sensory changes with the hand, with nocturnal symptoms. Motor findings, such as atrophy and weakness of median innervated muscles would be defined as Definite CTS. The Obstetrician will review the chart to complete the data for other obstetrical information. For the pilot study of RLS, the patient will answer questions on this topic during each of the sessions. Serial questionnaires and physical exams would be performed at the following intervals: 20-24 weeks gestation, 34-36 weeks gestation, and 6-10 weeks postpartum.

**Progress:** This protocol recently received review and approval by the IRB. No work was initiated on this study in FY 00.



## **Detail Summary Sheets**

**Pulmonary Disease & Critical Care Service,  
Department of Medicine**

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/033

**Status:** Ongoing

**Title:** A Multicenter, Randomized, Open-Label Study Comparing the Efficacy and Safety of Once Daily ORG 31540/SR90107A Versus Adjusted-Dose Intravenous Unfractionated Heparin (UFH) in the Initial Treatment of Acute Symptomatic Pulmonary Embolism (PE)

**Principal Investigator:** LTC William E. Caras, MC

**Department:** Medicine/Pulmonary&Critical Care

**Facility:** MAMC

**Associate Investigator(s):** COL Thomas A. Dillard, MC; LTC Bernard J. Roth, MC; LTC George N. Giacoppe Jr., MC; LTC Leonard E. Deal, MC; Erleen Spitsnoble, Pharm D; COL Dennis R. Beaudoin, MS

**Start Date:**  
1/25/1999

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
N/A

**Study Objective:** To demonstrate that an o.d. subcutaneous (s.c.) injection of ORG31540/SR90107A is at least as effective as adjusted-dose (aPTT, 1.5-2.5 x control) i.v. UFH in the initial treatment of patients with a confirmed diagnosis of acute symptomatic PE.

**Technical Approach:** This study treats acute pulmonary embolism with 2 different medications to determine if one medication is just as good as the other. After the patient has a confirmed diagnosis of acute pulmonary embolism (APE) and signs a consent form, that patient will be randomized to either standard therapy (UFH) or ORG31540/SR90107A. Patients will be treated with appropriate doses of either medication depending on the study arm to which they have been randomized, followed by a 90-day period of monitoring. The primary efficacy endpoint is the recurrence of a venous thromboembolism (VTE).

**Progress:** No patients have been enrolled in FY00 at MAMC.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/029

**Status:** Terminated

**Title:** A Prospective Study Using the Airway Occlusion Pressure (PO.1) To Predict the Outcome of Weaning From Mechanical Ventilation

**Principal Investigator:** COL Thomas A. Dillard, MC

**Department:** Medicine/Pulmonary&Critical Care

**Facility:** MAMC

**Associate Investigator(s):** MAJ James D. Pike, MC; LTC George N. Giacoppe Jr., MC; MAJ Francis J. Landry, MC; CPT Jeremy R. Blanchard, MC; MAJ Lewis L. Low, MC; CPT Kurt W. A. Grathwohl, MC

**Start Date:**  
12/17/1993

**Est. Completion Date:**  
May 94

**Periodic Review:**  
11/19/1999

**Study Objective:** The main objective of this study is to ascertain the usefulness of the PO.1 as a weaning parameter in predicting success or failure of patients upon extubation. The secondary objective is to validate the Rapid Shallow Breathing Index as described by Yang and Tobin.

**Technical Approach:** Weaning parameters will be obtained and documented by a Respiratory Care Practitioner (RCP) on patients in the surgical and medical ICU at MAMC. Individual progress toward weaning and extubation will be determined by the primary physician/team. When it is determined the patient is ready for extubation, a second set of weaning parameters will be obtained immediately prior to extubation. Weaning parameters will only be collected on patients at rest and who have not been stimulated within the prior 10 minutes. The parameters will be obtained by utilizing the Respiratory Mechanics Package on the Infrasonics Adult Star as required by MAMC policy. Only the data obtained from patients on the Infrasonic Adult STAR mechanical ventilator will be used so that our results are reproducible since other available ventilators do not easily measure the PO.1. The first 50 patient's will be used to form ROC curves to develop threshold values for the prediction of success or failure of extubation which can then be prospectively applied. A successful weaning/extubation will be defined as one in which the patient does not have to be reintubated within 24 hours.

**Progress:** Data collection had been completed by the original PI; however, the data was lost following his PCS to another institution. Attempts to continue work on this study at MAMC have not been possible due to time commitments; therefore, this study has been terminated due to the ETS of its current PI.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 96/138	<b>Status:</b> Terminated
<b>Title:</b> Active Inspiration/Expiration versus Tidal Volume Breathing During Transbronchial Biopsy		
<b>Principal Investigator:</b> COL Thomas A. Dillard, MC		
<b>Department:</b> Medicine/Pulmonary&Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Timothy R. Murray, MC; LTC Bernard J. Roth, MC; Suzette Gagnon-Bailey, M.D.; Ravi R. Ramakrishna, M.D.; CPT Kurt W. A. Grathwohl, MC		
<b>Start Date:</b> 8/16/1996	<b>Est. Completion Date:</b> Aug 97	<b>Periodic Review:</b> 9/28/2000

**Study Objective:** To compare yield, results and complications of two currently used techniques for transbronchial biopsy.

**Technical Approach:** All patients referred in the pulmonary clinic for bronchoscopy will be enrolled. Bronchoscopy will be performed in the usual manner. Patients will have a minimum of 6 transbronchial biopsies performed. They will be randomized to have the first three biopsies performed by either the active inspiration/expiration method or the tidal volume breathing method. After 3 biopsies are performed, the patient will be crossed over to the method not previously performed to obtain the next three biopsies. If more biopsies are needed, the attending physician can utilize any method at their discretion although the subsequent biopsy samples will not be included in data analysis. The attending pulmonologist or nurse will record the number of attempts for each and the appearance and quantity of sample grossly. Hemorrhage, pain, dyspnea, change in vital signs, and need for stopping the procedure will be recorded after each attempt. Two containers will be identified to the investigators although the examining pathologist will be blinded to the method performed. The pathologist will identify the number and size of samples in each as well as note the presence of alveolar tissue and the pathologic diagnosis if any. We will enroll 100 patients over one year. The differences between number of adequate samples and size will be compared using the paired student t-test. Other variables such as presence of alveoli and presence of complications (i.e. chest pain, bleeding, dyspnea, etc.) will be compared using the chi square test.

**Progress:** This protocol was terminated following the ETS of its principal investigator.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/055	<b>Status:</b> Terminated
<b>Title:</b> Telomerase Activity in Bronchial Washings, Pleural Fluid, Sputum, and Cerebrospinal Fluid (CSF)		
<b>Principal Investigator:</b> COL Thomas A. Dillard, MC		
<b>Department:</b> Medicine/Pulmonary&Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Ravi R. Ramakrishna, M.D.; LTC William E. Caras, MC; CPT Wade K. Aldous, MS; Rakesh Gaur, M.D.; B Brown; LTC Jerome B. Myers, MC		
<b>Start Date:</b> 3/20/1998	<b>Est. Completion Date:</b> Sep 98	<b>Periodic Review:</b> 7/25/2000

**Study Objective:** To determine the sensitivity and specificity of telomerase activity as an indicator of malignancy in non-surgical pleuro-pulmonary tissue samples, and CSF.

**Technical Approach:** Samples of lung (bronchial) washings and sputum samples obtained at bronchoscopy, pleural fluid and CSF will be compared with samples submitted for cytological and histological examination from patients with lung and chest wall masses as a screening and possibly diagnostic tool for primary lung cancers as well as metastatic cancers to the lung and chest wall. The results of these will be analyzed to determine the sensitivity and specificity of telomerase as a screening and diagnostic tool for lung cancer. This is a pilot study.

**Progress:** Data collected under this study was combined with the data from MAMC study #98086. This protocol was terminated at Madigan due to PCS/ETS of the original investigators.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 98/086                      **Status:** Completed

**Title:** Telomerase Activity in Non-surgical Specimens Obtained at Bronchoscopy and Fine Needle Aspiration

**Principal Investigator:** COL Thomas A. Dillard, MC

**Department:** Medicine/Pulmonary&Critical Care                      **Facility:** MAMC

**Associate Investigator(s):** LTC William E. Caras, MC; Ravi R. Ramakrishna, M.D.; CPT Wade K. Aldous, MS; CPT Tommy A. Brown, MC; MAJ David P. Tracy, MC; MAJ Sean P. Murray, MC; LTC Jerome B. Myers, MC; CPT Michael C. Royer, MC

**Start Date:**  
6/19/1998

**Est. Completion Date:**  
Feb 99

**Periodic Review:**  
6/22/2000

**Study Objective:** To determine the sensitivity and specificity of telomerase activity as an indicator of malignancy in non-surgical pleuro-pulmonary tissue samples.

**Technical Approach:** The type of samples submitted will be bronchial brushings, trans-bronchial biopsies, endobronchial biopsies and wang needle aspirates obtained during bronchoscopy. Other samples for evaluation will include pleural biopsies and fine needle aspirations of lymph nodes, chest and lung masses. The qualitative telomerase activity will be determined using the telomerase PCR ELISA kit supplied by Boehringer Mannheim. In those patients where there is activity an attempt will be made to quantitate the amount of activity. The telomerase activity will be compared with cytological and histological diagnosis from samples obtained by non surgical means and in those patients who undergo surgery with surgical samples.

**Progress:** Data on 90 samples from 80 subjects were collected during FY 99. The data from this study has been combined with that from MAMC study #98055. Detection of telomerase activity in thoracic malignancies appears feasible from clinical diagnostic specimens. Prevalence of telomerase activity by gel electrophoresis was similar in small cell and non-small cell samples. Further work on this protocol was terminated at MAMC, 27 Jul 00, due to PCS/ETS of the original investigators.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/143

**Status:** Ongoing

**Title:** A Phase I Safety, Tolerability, Acceptability and Microbial Kinetic Study of Topical IB-367 Gel and Rinse in Orally Intubated Patients Receiving Mechanical Ventilation (Protocol No. 09-001)

**Principal Investigator:** LTC George N. Giacoppe Jr., MC

**Department:** Medicine/Pulmonary&Critical Care

**Facility:** MAMC

**Associate Investigator(s):** LTC Leonard E. Deal, MC

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** Part I: To compare the tolerability of IB-367 Gel and Rinse and to determine the antimicrobial response following a single 9 mg and a single 30 mg oral administration of IB-367 Gel or Rinse in orally intubated patients receiving mechanical ventilation. Part II: To determine the most favorable regimen of IB-367 (safety, tolerability, dosage, and frequency of administration) that reduces the bacterial burden of the aerodigestive tract in orally intubated patients receiving mechanical ventilation.

**Technical Approach:** This is a multicenter, randomized clinical trial with two parts. Part I will not be initiated at MAMC. Based on the safety data and antimicrobial effect seen in both the Gel and Rinse formulations in Part I and the information obtained from nurses and patients regarding the acceptability, one formulation will be chosen for administration during Part II. Part II will evaluate the safety, tolerability, and antimicrobial effect of up to 4 IB-367 Study Drug Administration Regimens. Regimens are designed so that individual administrations of IB-367 will not exceed 30 mg, the total daily dose will not exceed 60 mg, and the interval between doses will be no less than every 4 hours. Part II of the trial will enroll up to 4 cohorts of 8 patients each. In each cohort 6 patients will receive up to 5 days of IB-367 administration and 2 patients will receive equal volumes of placebo. Each cohort will receive a different Study Drug Administration Regimen. Enrollment in each cohort will begin after the safety and antimicrobial data has been evaluated from the previous cohort. Each cohort will be monitored for AEs, particularly vasovagal and gastrointestinal events. Oral, oropharyngeal, and tracheal secretions will be collected and evaluated for antimicrobial effect. Secretion collection will occur around the first Study Drug Administration and then every 24 hours thereafter. The schedule of secretion collection will vary depending on the regimen. Antimicrobial response will be evaluated by comparing the number of CFUs in all samples before and after the Study Drug administration. If any patient develops pneumonia or other significant infections (e.g.: urinary tract infections, wound infections, and bacteremias) attempts will be made to clearly identify the causative organism.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/102

**Status:** Terminated

**Title:** The Effect of Saphenous Vein Versus Internal Mammary Artery Bypass on the Mortality and Morbidity of Severe Chronic Obstructive Pulmonary Disease Patients

**Principal Investigator:** CPT Brian T. McKinley, MC

**Department:** Medicine/Pulmonary&Critical Care

**Facility:** MAMC

**Associate Investigator(s):** LTC Bernard J. Roth, MC; CPT Viki J. Leefers, AN; CPT Jamia E. Howell, MC; COL Thomas A. Dillard, MC; CPT Steven W. Krause, MC; CPT Claire S. Jenkins, MC

**Start Date:**  
9/15/1998

**Est. Completion Date:**  
Aug 98

**Periodic Review:**  
7/27/1999

**Study Objective:** (1) To determine the effect the type of graft used has on the morbidity and mortality of patients with severe chronic obstructive pulmonary disease who undergo coronary artery bypass, (2) to re-examine the effect confounding variables have on COPD patients under CABG.

**Technical Approach:** Patients within the last five years with the diagnosis of COPD undergoing CABG, and a second group of sex and age matched non-COPD patients as controls will be computer selected for this retrospective cohort study. Confounding variables which will be examined include preoperative bronchodilator usage and cardiac ejection fraction, total bypass pump time, active smoking, number of vessels bypassed, type of bypass whether left main, left anterior descending artery (LAD) or other, placement of a thoracostomy type, steroid usage, abnormal preoperative chest x-ray, higher American Society of Anesthesiologist class, and comorbid disease as defined as the preoperative existence of diabetes, hypertension, and renal disease.

**Progress:** This protocol was reported as terminated, 26 Sep 00, due to the PCS of its original PI and loss of data collected during his move.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/132

**Status:** Ongoing

**Title:** Respiratory Care Team to Decrease the Misuse of Metered Dose Inhalers in Hospitalized Patients

**Principal Investigator:** LTC Bernard J. Roth, MC

**Department:** Medicine/Pulmonary&Critical Care

**Facility:** MAMC

**Associate Investigator(s):** COL Thomas A. Dillard, MC; Michael G. Winter, RRT; Nora A. Regan; CPT John J. Mullan, MC; CPT Michael W. Quinn, MC

**Start Date:**  
9/19/1997

**Est. Completion Date:**  
Mar 96

**Periodic Review:**  
8/22/2000

**Study Objective:** To determine if a respiratory team teaching proper metered dose inhaler (MDI) use to inpatients will improve the observed rate of proper MDI use at Madigan Army Medical Center (MAMC).

**Technical Approach:** In this study, a pulmonologist will interview 60 inpatients prescribed an MDI and observe their MDI technique to establish a baseline rate of misuse. Then a respiratory care team will receive a daily list from Pharmacy on all patients newly prescribed an MDI. They will provide direct teaching to the patients on correct use of their MDI. After the teaching program has been in place for 2- 6 weeks the same pulrnonologist will interview 60 more patients and observe their MDI technique to establish the rate of misuse after the intervention. The patient will be asked if they have received education and this will be correlated to the chart documentation of education by the Respiratory Therapist. The major endpoint will be the change in the rate of MDI misuse observed.

**Progress:** 90 patients have been enrolled in this study at MAMC. This study is halfway through the second phase. Patient enrollment continues.

### Detail Summary Sheet

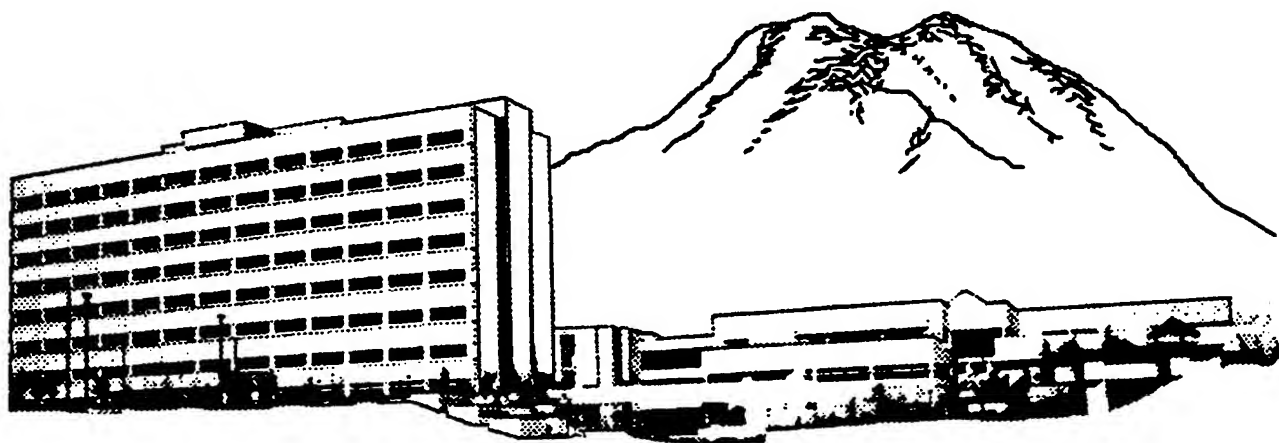
<b>Date:</b> 29 Sep 00	<b>Number:</b> 90/099	<b>Status:</b> Ongoing
<b>Title:</b> Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure		
<b>Principal Investigator:</b> CPT Samara Rutberg, MC		
<b>Department:</b> Medicine/Pulmonary&Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC William H. Cragun, MC; CPT Stephen M. Salerno, MC; CPT Donald M. Collins, MC; LTC Bernard J. Roth, MC; CPT Jennifer E. Jorgenson, MC		
<b>Start Date:</b> 8/17/1990	<b>Est. Completion Date:</b> Jun 96	<b>Periodic Review:</b> 6/27/2000

**Study Objective:** To determine if the albumin gradient is a more effective criterion than Light's criteria to distinguish transudates from exudates in patients with congestive heart failure that have been treated with diuretics.

**Technical Approach:** Fifteen patients with clinically suspected congestive heart failure and chest radiograph evidence of pleural effusion will be studied. A thoracentesis to remove 50 cc of fluid will be performed and the following laboratory tests will be done on the fluid: albumin, total protein, glucose, LDH, bilirubin, cell count with cyto-spin differential, gram stain, and routine culture. A simultaneous sample of serum will be measured for albumin, total protein, LDH, bilirubin, and glucose. After three to five days of therapy for the congestive heart failure a repeat chest radiograph with bilateral decubitus view will be done. If pleural fluid persists, a repeat thoracentesis and laboratory tests will be done. If no fluid persists after three to five days, then the patient will be dropped from the study. Bilirubin ratio will also be assessed. The classification of the patients as exudate or transudate by serum effusion, bilirubin ratio, and Light's criteria will be compared between the two thoracentesis. McNemar's test for matched-pair data will be used to compare the albumin gradient results to Light's criteria.

**Progress:** One patient enrolled in this study in FY00, for a total of 42. Other patients have been evaluated although they were found to have transudative effusions possibly for other reasons, i.e., renal failure, and had to be excluded. Subject recruitment continues.





## Detail Summary Sheets

Rheumatology Service,  
Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/078	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Prograf (Tacrolimus) in the Treatment of Rheumatoid Arthritis in Patients Who Have Failed One or More Disease-Modifying Antirheumatic Drugs		
<b>Principal Investigator:</b> LTC Thomas L. Irvin, MC		
<b>Department:</b> Medicine/Rheumatology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ David R. Finger, MC; MAJ Leslie W. Jackson, MC		
<b>Start Date:</b> 6/22/1999	<b>Est. Completion Date:</b> Jun 00	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** This protocol is designed to evaluate the efficacy and safety of the immunosuppressant tacrolimus in RA patients who are either resistant or intolerant of one or more DMARDs.

**Technical Approach:** This will be a 6 month multi-center, randomized, double-blind, placebo controlled study of adult patients, of either gender, with a diagnosis of rheumatoid arthritis for at least 6 months. Eligible patients will have demonstrated either resistance to or intolerance of one or more DMARDs. A total of 450 patients from approximately 50 centers will be randomized, with a maximum of 36 patients per center. Patients will be assigned to either the DMARD resistant or the DMARD intolerant stratum prior to randomization. Randomization to the three treatment arms will be at 1:1:1, tacrolimus (2 mg/day), tacrolimus (3 mg/day), or placebo respectively within each stratum at each center.

The primary efficacy endpoint will be the composite American College of Rheumatology (ACR) 20 success at six months for the combined 2 mg and 3 mg tacrolimus groups as compared to placebo. If the combined treatment group response is statistically significantly different from the placebo group response, then the pairwise comparisons between the placebo and the individual tacrolimus groups will be performed. Secondary efficacy endpoints are the ACR 20, 50, and 70 response rates at the end of the treatment, and the evaluation of change from baseline for the individual components of the ACR composite at end of treatment.

**Progress:** Two patients have been enrolled in this study at MAMC. No adverse events have been reported. Patient enrollment continues.

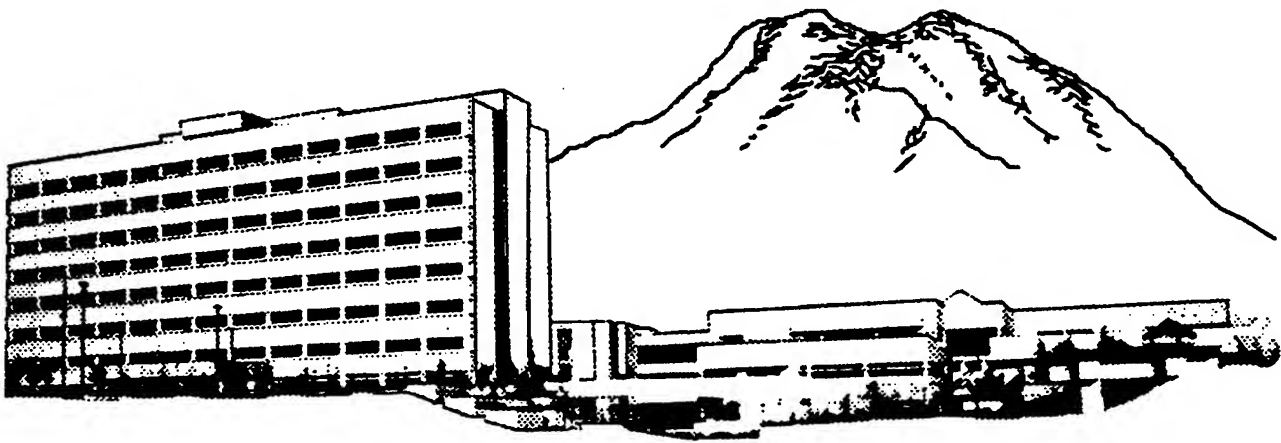
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/079	<b>Status:</b> Ongoing
<b>Title:</b> An Open-Label, Long-Term Study to Evaluate the Safety of Prograf (tacrolimus) for the Treatment of Rheumatoid Arthritis		
<b>Principal Investigator:</b> LTC Thomas L. Irvin, MC		
<b>Department:</b> Medicine/Rheumatology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ David R. Finger, MC; MAJ Leslie W. Jackson, MC		
<b>Start Date:</b> 6/22/1999	<b>Est. Completion Date:</b> Jun 02	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** The primary objective of this study is to evaluate the long-term safety of Prograf in rheumatoid arthritis patients. A secondary objective of the study is to evaluate long-term efficacy of Prograf in RA patients.

**Technical Approach:** This will be a 12 month open-label, non-comparative, multi-center study. Eligible patients will have an RA diagnosis of at least six months duration and, in the investigator's opinion, require the use of a DMARD. A total of approximately 300 patients who have participated in previous Fujisawa protocols and approximately 500 patients who are entering this study directly will be enrolled at approximately 80 centers. All patients will receive a total daily dose of 3 mg of tacrolimus. Adverse events, including clinically significant laboratory abnormalities, will be recorded on the Case Report Forms. Treatment emergent adverse events during the 12 months of the open-label treatment will be determined and will be the primary assessment of risk. ACR 20, 50, and 70 will be assessed at 3, 6, 9, and 12 months as secondary endpoints of the study.

**Progress:** Two patients have been enrolled in this study at MAMC. No adverse events have been reported. Patient enrollment continues.



## Detail Summary Sheets

Department of Ministry and Pastoral Care

### Detail Summary Sheet

Date: 29 Sep 00	Number: 200/070	Status: Completed
Title: Chaplain Intervention with Loneliness in the Military		
Principal Investigator: CPT Doyle Coffman, CH		
Department: Ministry & Pastoral Care	Facility: MAMC	
Associate Investigator(s): None.		
Start Date: 5/23/2000	Est. Completion Date: May 00	Periodic Review: N/A

**Study Objective:** To develop intervention programs that can be used with the military population based on a pilot study of loneliness among the patient population and the effects of spirituality of the severity of loneliness.

**Technical Approach:** This study issues questionnaires to willing patients and nurses on various MAMC wards. Included in the questionnaire is the UCLA Loneliness Scale. Answers from the surveys will aid the chaplains in structuring a Loneliness Intervention Program.

**Progress:** The UCLA Loneliness Scale (version 3) and the Loneliness Survey 001 was administered to 20 staff members at MAMC and 20 patients, 10 male and 10 female, ages 18-72, selected by convenience for the survey. Data collected was only a pilot portion and not sufficient to draw adequate conclusions. Results: of staff members indicated that the staff did not feel apart of a group of friends, but they felt they had little in common with those around them. The survey conducted on the patients showed that they seem to feel isolated from others and indicated that the patients feel they do not share interest and ideas with those around them. The survey also showed that patients felt they were alone. As a whole, males scored higher on the loneliness scale than females, which was unexpected as males generally have a lower score on the scale than females. The highest rates for loneliness were indicated among the 62 years and older group. There seemed to be little difference between married patients and those widowed, divorced, or single. Attending nurses surveyed indicated that the highest loneliness scores were seen with lower family support to the patient. They also cited an overwhelming lack of social support in all loneliness scores of patients. In looking at how the attending nurse perceived the patient's attitude, the highest loneliness scores indicated that the patient was shy or depressed. For the most part, those patients who were taking longer to recover also scored higher on the loneliness scale. Nurses observations also showed that those patients scoring high on the loneliness scale never expressed their faith openly. Religious preference was not included in the demographics in order to get an unbiased approach to the correlation between faith in God and loneliness. Conclusion: Although the research is quite limited and should only be acknowledged as a pilot study, one can see the correlation between loneliness and health.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/071	<b>Status:</b> Completed
<b>Title:</b> The Chaplain's Role on the Hospital Ethics Committee (HEC)		
<b>Principal Investigator:</b> CPT Thomas Eddy, CH		
<b>Department:</b> Ministry & Pastoral Care	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
May 00

**Periodic Review:**  
N/A

**Study Objective:** To identify the role and influence of the chaplain on the hospital ethics committee.

**Technical Approach:** Army Medical Center Hospital Ethics Committee (HEC) members will be administered an anonymous and voluntary questionnaire about HEC membership and the chaplain's role, if any. All Army Medical Center chaplains will be given a two-part anonymous questionnaire about their ethics discussions concerning patients and others, their training in ethics, etc.

**Progress:** 31 chaplains and 20 non-chaplain HEC members completed and returned the surveys. **Results:** The chaplain is able and expected to bring ethical, theological and moral light to the case or policy being discussed. The chaplain is able to concentrate on the spiritual issues that are presented by the patient and the family, not just the philosophical issues raised by the case. The chaplain can provide support to the other members of the committee who might overlook the spiritual significance of medical ethics choices. The committee also looks upon the chaplain as a member who has very likely already been in contact with the family and the medical team, which is welcomed by the committee and considered vital to the analysis of the case. Another major issues considered when discussing medical ethics decisions is that of quality of life. Surveys showed that the chaplain can bring to light other issues such as the sanctity of life or the intrinsic value and learning gained in suffering, which is often overlooked in today's materialistic, utilitarian world view. **Conclusion:** The chaplain is a key person on the HEC committee with much influence, providing insights on the patient's world view and spiritual overtones that are involved, especially in life and death issues and bringing to light moral ramifications that might not otherwise be addressed. The chaplain can be a key link between the committee, the medical staff and those who are involved in the case. (A complete abstract is available).

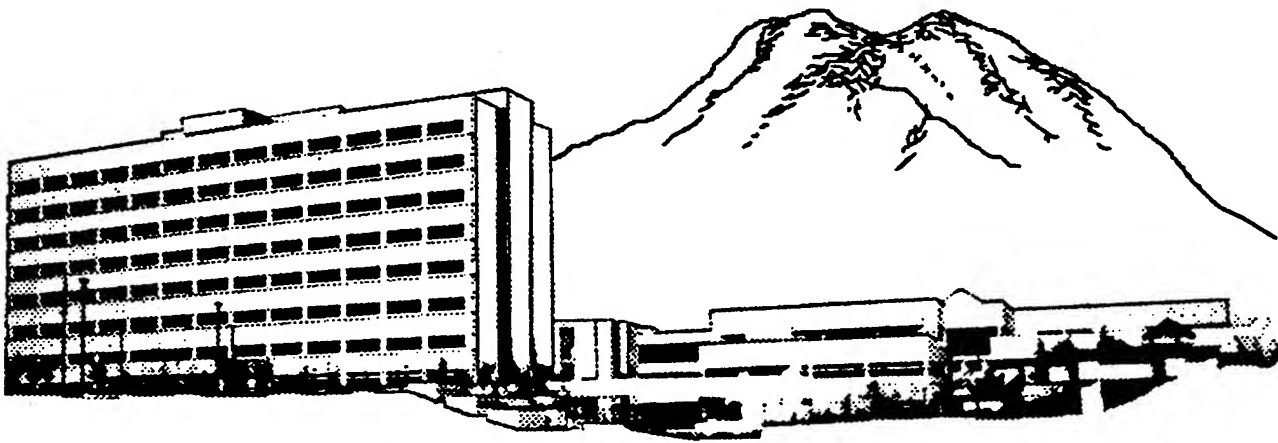
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/069	<b>Status:</b> Completed
<b>Title:</b> The Dying, Our Finest Teachers: Helping Chaplains Understand Their Role in Providing Pastoral Care to the Dying		
<b>Principal Investigator:</b> CPT William Green, Jr., CH		
<b>Department:</b> Ministry & Pastoral Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start Date:</b> 5/23/2000	<b>Est. Completion Date:</b> May 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine what the dying can teach chaplains and caregivers so that they can pastor and effectively care for patients during their final days.

**Technical Approach:** Surveys will be administered to 10 terminally ill and 10 non-terminally ill patients. Participation will be stressed to be voluntary. Responses to questions will be compiled and described.

**Progress:** Protocol has been reported as completed; however, an abstract of the findings for this study was not available at the time of the PCS of its PI.



## Detail Summary Sheets

Department of Nursing



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/116	<b>Status:</b> Ongoing
<b>Title:</b> Publishing Practices and Perceptions by Registered Nurses at a Military Medical Center			
<b>Principal Investigator:</b> LTC Wynona M. Bice-Stephens, AN			
<b>Department:</b> Nursing		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Elizabeth A. Mittelstaedt, AN			
<b>Start Date:</b> 8/22/2001	<b>Est. Completion Date:</b> Mar 01	<b>Periodic Review:</b> N/A	

**Study Objective:** (1) To describe publishing practices by Registered Nurses as a military medical center, (2) To identify perceptions of aspects of publishing by Registered Nurses at a military medical center, and (3) To identify whether nurses are encouraged to publish by internal or external motivators.

**Technical Approach:** This study will survey registered Nurses to determine their perceived barriers to publication. Based on results of the questionnaires, a publication workshop will be designed for Department of Nursing personnel.

**Progress:** No work has been done on this protocol in FY00. Protocol is to be initiated January 2001.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/126      **Status:** Ongoing

**Title:** The Effect of Marshmallow Consumption on the Quantity of Effluent During an Appliance Change in Individuals with an Ileostomy

**Principal Investigator:** LTC Wynona M. Bice-Stephens, AN

**Department:** Nursing      **Facility:** MAMC

**Associate Investigator(s):** LCDR Kerri S. Pegg, NC, USN

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** To compare the effect of consumption of marshmallows versus non-consumption of marshmallows to the quantity of effluent expressed in individuals with an ileostomy during a simulated appliance change.

**Technical Approach:** Each of the 10 subjects will collect the effluent four times during simulated appliance changes. For two of the simulations, they will collect effluent as "control", meaning that they will not eat marshmallows prior to changing the appliance. For two simulations, subjects will eat the marshmallows prior to changing the appliance, and collect the effluent during the appliance change. Results from the "control" versus "intervention" will be evaluated to determine if there was more or less effluent when marshmallows were consumed prior to appliance change simulation.

**Progress:** This protocol recently received review and approval by the IRB; however it has not received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/136

**Status:** Ongoing

**Title:** Prevention of Hypertension in the United States Army: A Descriptive Correlational Study on Dietary Habits of Junior Enlisted Soldiers Living at Fort Lewis, WA

**Principal Investigator:** LTC Wynona M. Bice-Stephens, AN

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** CPT Jean Jones, AN; Susanna Cunningham; CPT Michelle D'Amico, SP

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Jan 01

**Periodic Review:**  
N/A

**Study Objective:** 1. To document the macronutrient and micronutrient intake of soldiers living at Fort Lewis, WA, specifically sodium, Vitamin C, omega 3 fatty acids, and the number of fruits and vegetables per day

2. To compare intake of soldiers with a diet that decreases the risk of developing hypertension

3. To document the general dietary habits of soldiers living at Fort Lewis, Washington.

**Technical Approach:** Subjects will be recruited to participate in the study as their unit participates in the Corporate Wellness Program. Subjects will complete three questionnaires including demographic data, dietary habits, and food frequency.

**Progress:** This protocol recently received review and approval by the IRB; however it has not received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/137	<b>Status:</b> Ongoing
<b>Title:</b> Development and Evaluation of the Military Nursing Moral Distress Scale		
<b>Principal Investigator:</b> LTC Wynona M. Bice-Stephens, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Ann Hurley, AN; Sara Fry; COL Barbara Jo Foley, AN		
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> May 01	<b>Periodic Review:</b> N/A

**Study Objective:** The ultimate objective of this program of research is to minimize moral distress in military nurses during crisis military deployments. Crisis deployment refers to that time when the officer has been ordered to support an operation off station (and perhaps out of country) to provide nursing care during a military operation, humanitarian and/or peacekeeping mission. This project will develop and evaluate an instrument to measure the moral distress (MMDS) of nurse officers in the US Army. Moral Distress is defined as the negative balance between a nurse's moral judgment and the opportunity to implement that judgment in nursing actions.

**Technical Approach:** Subject in this study will fill out a series of questionnaires indicating their levels of moral distress.

**Progress:** This protocol recently received review and approval by the IRB; however it has not received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/022      **Status:** Terminated

**Title:** Nurse Practitioner Manager Outpatient Heart Failure Program

**Principal Investigator:** MAJ Theresa A. Horne, AN

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** Lori A. Loan, PhD

**Start Date:**  
1/26/1999

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
N/A

**Study Objective:** To determine the best managed care model for providing care to patients with congestive heart failure.

**Technical Approach:** This study will use a randomized controlled clinical trial with two parallel arms to compare a cardiology NP-managed heart failure program to standard care provided by a primary care provider and cardiologist. A holistic nursing perspective and the Health Related Quality of Life (HRQL) Model provide the framework for conceptualization and measurement of patient and utilization outcomes. Primary outcomes are hospitalization, ER visits, clinic visits and disease specific quality of life. Secondary outcomes include functional status, self-perceived functional status, general health, health care provider adherence to effective drug therapy, self reported dietary sodium intake, deviation in weight, self-reported symptom scores, hospitalized days and cost for health care utilization. Data will be compiled using medical record reviews, patient logs, general and disease-specific instruments of HRQL, and telephone interviews. Chi-square, t-test, and Mann Whitney U tests will be used to compare group outcomes.

**Progress:** This study was terminated due to lack of funding.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/047	<b>Status:</b> Ongoing
<b>Title:</b> Prone Position and the Pattern of Oxygenation in Acute Lung Injury Patients		
<b>Principal Investigator:</b> Lori A. Loan, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Janet R. Harris, AN; Kathleen Vollman; LTC George N. Giacoppe Jr., MC; MAJ Mary S. McCarthy, AN		
<b>Start Date:</b> 3/28/2000	<b>Est. Completion Date:</b> Dec 03	<b>Periodic Review:</b> N/A

**Study Objective:** To examine the pattern of oxygenation in 60 patients with acute lung injury (ALI)/adult respiratory distress syndrome (ARDS) who undergo a 4-hour prone positioning trial and to develop evidence-based guidelines for a prone positioning protocol regarding safety, timing, and frequency of the intervention for patients with ALI or ARDS.

**Technical Approach:** Informed consent will be obtained from the patient or surrogate prior to participation in the study. Patient ventilator settings, positive end-expiratory pressure (PEEP) and inspired oxygen fraction (FiO<sub>2</sub>), will be established by the patient's physician according to the clinical needs of the patient. During the data collection periods for this study, the ventilator settings will remain unchanged. An Acute Lung Injury Score (Murray et al., 1988) will be assessed for each subject to further delineate the severity of acute pulmonary damage

Prior to data collection all equipment will be calibrated according to the manufacturer's recommendations. The arterial line will be calibrated and leveled to the subject's phlebostatic axis (Boggs & Wooldridge-King, 1993). Baseline supine measurements will occur after the subject has been in the supine position for at least one hour and just prior to turning the subject to the prone position. Following site visits to both facilities by the Consultant who is the developer and an expert in the device to be used for the intervention, trained teams will be identified. The subject will be turned to the prone position. PaO<sub>2</sub>/FiO<sub>2</sub> will be measured every hour for the 4 hours the subject is in the prone position. The subject will remain in the prone position for 4 hours unless the subject does not tolerate the prone position or has an emergency (loss of airway or central access, cardiopulmonary resuscitation, hemodynamic instability). Following initial measurements in the baseline supine position, measurements will be conducted at 1 hour intervals while the subject is in the prone position and 1 & 2 hours after returning to the supine position.

Subject demographics that will be collected include: age, gender, diagnoses, etiology of acute lung injury, parenteral and enteral nutrition, date of admission to ICU, duration of time since first diagnosed with ALI, days of mechanical ventilation before initial prone trial, Acute Lung Injury Score, and severity of illness as measured by the APACHE II scoring tool.

**Progress:** This protocol has not yet started to enroll patients at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/095

**Status:** Ongoing

**Title:** Expectations of Military Health Care: An Inductive Analysis

**Principal Investigator:** Lori A. Loan, PhD

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** COL Bonnie M. Jennings, AN; Debra DePaul, RN

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 02

**Periodic Review:**  
N/A

**Study Objective:** To acquire empirical evidence for use in reforming military health care, for the purpose of improving patient satisfaction and quality.

**Technical Approach:** Focus groups consisting of active duty personnel and family members of active duty personnel, will be utilized in this study to present customer satisfaction/expectation questionnaires to recipients of military medical care and use the results to analyze both real and perceived strengths and weakness of the Military Health System. Focus groups specific to health care personnel will also be conducted to explore differences between consumer expectations and health care personnel perceptions of the care delivery process.

**Progress:** This study has not yet begun at MAMC. Investigators have submitted the study for approval by Womack Army Medical Center IRB.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/068

**Status:** Completed

**Title:** Effects of Stress Responses on Wound Healing

**Principal Investigator:** Lori A. Loan, PhD

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** JoAnne D. Whitney, Ph.D., RN; Margaret M. Heitkemper, Ph.D.; Stacey L. Heiner, BSN, RN; MAJ Susanne J. Clark, AN

**Start Date:**  
3/21/1997

**Est. Completion Date:**  
Sep 00

**Periodic Review:**  
3/23/1999

**Study Objective:** Compare measures of preoperative and postoperative psychological stress, SNS and HPA activation (STAI, RIES, PSQ-III GSS, urinary norepinephrine, epinephrine and cortisol) in subjects experiencing minor (e.g., outpatient arthroscopic) and major (e.g., total knee arthroplasty) surgical procedures.

**Technical Approach:** The proposed study will use a prospective, correlational design to explore relationships between pre and postoperative psychologic and physiologic stress and the defined wound healing indices. The study will enroll a total of 96 subjects over a three year period from populations experiencing minor and major orthopedic knee surgery. The relationship between each preoperative and postoperative measure of stress and each wound healing measure will be evaluated with the Pearson product moment correlation coefficient. Repeated measures analysis of variance will be used to compare the stress experienced by patients undergoing major surgery to those undergoing minor surgery at the eight times of measure.

**Progress:** Recruitment for this study was completed in December 1999. Biochemical analysis of ePTFE samples has been completed. Results of the biochemical analyses were received July 2000. This study is currently in the data analysis and interpretation phase. No conclusions have been drawn at this time.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 98/044	<b>Status:</b> Ongoing
<b>Title:</b> Physical Activity and Exercise in AD Female Soldiers			
<b>Principal Investigator:</b> Lori A. Loan, PhD			
<b>Department:</b> Nursing		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Debra DePaul, RN; LTC Laura R. Brosch, AN; COL Melissa A. Forsythe, AN			
<b>Start Date:</b> 2/20/1998	<b>Est. Completion Date:</b> Oct 98		<b>Periodic Review:</b> 1/25/2000

**Study Objective:** To examine the physical activity levels and habitual exercise patterns of active duty female soldiers and to identify factors that influence those habits in hopes of producing information to be used to improve the health of female soldiers.

**Technical Approach:** Each subject will complete an initial survey and APFT scores will be obtained for each service member consenting to be in the study. Focus groups will then explore the issues among subjects identified as belonging to subgroups at risk for low exercise participation.

**Progress:** No subjects were enrolled in FY00; however, 1103 subjects had been enrolled in FY99, with data analysis continuing on surveys collected. Four focus groups were conducted, content analysis of focus group themes continues. During FY00, Dr. Lori Loan assumed the role of PI for this study, due to the PCS of LTC Laura Brosch to WRAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 98/053      **Status:** Ongoing

**Title:** Improving Soldier Access to Urinary Incontinence Therapy

**Principal Investigator:** Lori A. Loan, PhD

**Department:** Nursing      **Facility:** MAMC

**Associate Investigator(s):** LTC Ann M. V. Bianchi, AN; LTC (Ret) Richard A. Sherman, MS

**Start Date:**  
1/16/1998

**Est. Completion Date:**  
Sep 98

**Periodic Review:**  
1/25/2000

**Study Objective:** This study aims to compare access to care and patient satisfaction with care for female soldiers receiving biofeedback treatment for exercise-induced urinary incontinence in the troop medical clinic environment with those receiving similar treatments at a medical center.

**Technical Approach:** All subjects interested in participating in the study will be screened for evaluation of the lower urinary tract. If inclusion criteria is met, the subject will be randomized to treatment at either the TMC or MAMC and be scheduled for treatment visits every 2 weeks for 12 weeks. During the first visit, demographic and descriptive information will be gathered and subjects will learn how to do Kegel exercises using biofeedback. Subjects will be asked to keep daily logs and to practice the Kegel exercises for twenty minutes two times a day.

Subsequent visits to the treatment center will be to encourage continuation and the keeping of daily logs. At the final visit more demographic and descriptive information will be asked and a Patient Satisfaction Questionnaire will be filled out by each subject. The portable biofeedback equipment will be used to evaluate Kegel performance during this final visit.

**Progress:** As of 1 July 00, screening tools had been returned from 2,499 female soldiers at Fort Lewis, with 917 returning the survey. 131 indicated they wanted treatment for urinary incontinence. 64 were eligible and consented. 53 started the intervention and 30 have completed the intervention. A fourth mailing of the screening tool is underway for study recruitment.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 98/107	<b>Status:</b> Ongoing
<b>Title:</b> Nurses Influence on Patient Outcomes in US Army Hospitals			
<b>Principal Investigator:</b> Lori A. Loan, PhD			
<b>Department:</b> Nursing		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Barbara Jo Foley; Dr. Carolyn C. Kee; Dr. Ptlene Minick; Dr. Susan Harvey; COL Bonnie M. Jennings, AN			
<b>Start Date:</b> 9/15/1998	<b>Est. Completion Date:</b> Sep 99		<b>Periodic Review:</b> 8/22/2000

**Study Objective:** To describe patient outcomes in active duty personnel, military retirees, and military dependents, associated nursing organizational structures and processes; and hospital characteristics.

**Technical Approach:** Interviews, questionnaires and short answer surveys will be used to gather information on (1) patient outcomes while in the hospital to include the occurrence of adverse events such as injury-sustaining falls, length of stay, and severity-adjusted mortality; (2) following discharge from the hospital, outcomes include patient satisfaction with nursing care, satisfaction with how symptoms were managed, and functional health status. (3) Nursing organizational structures include factors such as nursing practice model, nursing skill mix, and the education and experience level of registered nurses (RN); and (4) nursing organizational processes include RN job satisfaction, the degree of autonomy in nursing practice or the discretionary judgement accorded nurses in the work environment, the level of RN and physician collaboration, the degree of clinical expertise, and the extent to which an ethical work environment is present.

**Progress:** 57 subjects were enrolled in FY00 for a total of 205 subjects enrolled at MAMC. Subject population includes active duty, retirees and dependents. During FY00, Dr. Lori Loan assumed the role of PI for this study, due to the PCS of LTC Laura Brosch to WRAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/025	<b>Status:</b> Terminated
<b>Title:</b> The Effects of Postoperative Supplemental Oxygen on Tissue and Wound Healing		
<b>Principal Investigator:</b> Lori A. Loan, PhD		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> JoAnne D. Whitney, Ph.D., RN; Stacey L. Heiner, BSN, RN; LTC Pamela J. Hildreth, AN; CPT Jeannie M. Padilla, MC; Candace Plumlee; LTC Jerome B. Myers, MC; Kathleen A. Clary, RN		
<b>Start Date:</b> 1/26/1999	<b>Est. Completion Date:</b> Jun 01	<b>Periodic Review:</b> 1/25/2000

**Study Objective:** Compare the effects of 36 hours of supplemental oxygen therapy provided postoperatively to patients having surgery to management of patients without supplemental oxygen on wound healing in test wound samples and subcutaneous tissue oxygen levels. Compare the incidence of wound complications between the two groups evaluated in the surgical wound on postoperative days 2 and 7. Compare clinical healing outcomes and describe complications that occurred in the two groups during the first 30 days post surgery.

**Technical Approach:** This study uses a randomized, two group, experimental repeated measures design. 160 essentially healthy subjects with a need for cervical spinal fusion and/or excision of a cervical intervertebral disc or excision of a lumbar intervertebral disc(s), will be recruited for the study. Subjects will be randomly assigned to receive only room air (control group) or supplemental oxygen at 28% via nasal cannula for 36 hours postoperatively (treatment group). PscO<sub>2</sub> will be measured at Hour 1, 18 and 36 using a tonometer/sensor system. Wound healing is evaluated by analysis of tissue cellularity and hydroxyproline from a tissue sample obtained from a small, polytetrafluoroethylene tube placed subcutaneously and removed on the 7th postoperative day. Wound complications/infections will be evaluated using the Wound Registry. Differences between groups will be tested using Analysis of Variance for repeated measures, Wilcoxon Rank Sum test, and Chi-square.

**Progress:** This study was terminated at MAMC, 29 Sep 00, as the patient population chosen routinely leaves the PACU breathing "room air," therefore, no patients were able to meet inclusion criteria for randomization. This study will be rewritten using a different patient population, and submitted for IRB approval.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/028	<b>Status:</b> Ongoing
<b>Title:</b> Factors Associated with Preventable Hospitalization in Older Military Retirees			
<b>Principal Investigator:</b> Lori A. Loan, PhD			
<b>Department:</b> Nursing		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Bonnie M. Jennings, AN; Suzanne K. Wilson, MSN, RN; LTC Laura R. Brosch, AN			
<b>Start Date:</b> 2/23/1999	<b>Est. Completion Date:</b> Jun 01		<b>Periodic Review:</b> 1/25/2000

**Study Objective:** To prospectively assess the relationship between patient-specific characteristics and the likelihood of preventable hospitalization for Tricare Senior Prime enrollees.

**Technical Approach:** All 3,620 Madigan Army Medical Center Tricare Senior Prime enrollees will be surveyed to obtain baseline predisposing (age, gender, race, education, living arrangements), enabling (income, tangible social support, perceptions of regular source of care, transportation, transportation time) and need factor (perceived physical health status, perceived mental health status, perceived functional limitations, chronic illnesses, past hospital use) data. These data will subsequently be linked to hospitalization data prospectively collected for the 12 month period following the survey. Each study participant's hospital use will be classified into one of three categories: (1) no hospital admissions, (2) at least one potentially preventable hospitalization, or (3) hospitalized, but not for a potentially preventable condition.

Descriptive statistics will be used to profile the sample in terms of the factors under study and summarize the frequency of occurrence of each type of hospital use. Multivariate polytomous logistic regression will be used to identify predisposing, enabling and need factors associated with the likelihood of potentially preventable hospitalization.

**Progress:** Data collection for the 3620 participants who have agreed to be in this study is scheduled to be completed by May 2001. During FY00, Dr. Lori Loan assumed the role of PI for this study due to the PCS of LTC Laura Brosch to WRAMC.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 99/029	Status: Terminated
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**Title:** Evaluation of the Clinical Status and Resource Utilization of Ventilated Patients with Acute Respiratory Failure in Intensive Care Units via a Longitudinal Observational Outcomes Database

**Principal Investigator:** Lori A. Loan, PhD

Department: Nursing	Facility: MAMC
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**Associate Investigator(s):** MAJ Mary S. McCarthy, AN

**Start Date:**  
2/23/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
3/6/2000

**Study Objective:** (1) To develop and maintain a detailed, longitudinal computer database of data on clinical and resource use outcomes in ventilated patients with acute respiratory failure, (2) to obtain a sample size of sufficient magnitude to permit statistically significant clinical and economic analyses, (3) to describe existing patterns of clinical management across a broad patient sample, (4) to use these data to conduct cohort studies that investigate in-depth patient outcomes in acute respiratory failure, including the prevalence of infectious complications and prolonged mechanical ventilation, (5) to identify treatment protocols associated with improved outcomes in patients with acute respiratory failure, and (6) to identify patient characteristics and treatment variables predictive of optimal or poor outcomes.

**Technical Approach:** This is a non-interventional study in which 150 subjects will be enrolled from participating sites over a one-year period of time. Chart review and direct observation will be used to collect demographic, clinical, and hospital data. Potential subjects will be identified by the PI during morning rounds in the ICU. Once it is determined that the patient meets the eligibility criteria the patient will be enrolled in the data collection group. The majority of data collection will be completed once the subject has been discharged; however, subject identification and documentation of processes that rely on direct observation must be done while the subject is in the ICU (e.g. rotational therapy). Analyses of these data may permit identification of interventions or patterns of patient care that are associated with a lower rate of respiratory infection, a shorter average ventilator time or other favorable outcomes in this high risk population.

**Progress:** This study was terminated, 29 Dec 99, per the study sponsor, no reason given. A total of 85 subjects were enrolled and evaluated at MAMC and data submitted as requested.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/110

**Status:** Ongoing

**Title:** The Effects of Using Four Different Missing Data Imputation Methods on the Psychometric Property of the SF36

**Principal Investigator:** Lori A. Loan, PhD

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** Qiuping Zhou, MS, RN; LTC Laura R. Brosch, AN; 1LT Janet L. Hyers, AN

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
10/24/2000

**Study Objective:** The purpose of this study is to determine the effects of using four different missing data imputation methods on the psychometric property of SF36, for different sample sizes, different length of the questionnaire, and different percentage of missing data.

**Technical Approach:** This is a secondary data analysis. An existing data set with SF36 items included will be used to perform the simulations. The outcomes include the reliability and factor structure of the SF36 measure. Variables manipulated include (1) imputation methods (person mean, item mean, regression, and EM algorithm replacement), (2) length of the instrument (36 versus 12 items), (3) percentage of missing data (0%, 5%, 10%, 20%, and 30%) and (4) sample sizes (large, medium, and small).

Data collected from 2800 patients in a military organization. SPSS 8.0 will be employed to analyze the data. Reliability and factor analysis will be performed on data sets with varying conditions. The results will be compared and summarized. Replacing methods with the minimum effect on the psychometric performance of the SF36 will be identified.

**Progress:** Data for this study has been cleaned and separated into subsets for analysis. Currently in data analysis phase.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/076	<b>Status:</b> Completed
<b>Title:</b> Gastric/Jejunal Feeding: Nutritional Outcomes and Pneumonia		
<b>Principal Investigator:</b> MAJ Mary S. McCarthy, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Bernard J. Roth, MC; CPT Kurt W. A. Grathwohl, MC; 1LT Faith U. Watanabe, SP; MAJ Susanne J. Clark, AN		
<b>Start Date:</b> 5/17/1996	<b>Est. Completion Date:</b> Sep 98	<b>Periodic Review:</b> 4/27/1999

**Study Objective:** 1) To compare nutritional outcome between patients randomized to gastric or jejunal tube feeders as measured by: a) daily caloric intake, b) subjective global assessment, c) biochemical parameters, d) delayed cutaneous tests and e) indirect calorimetry. 2) To compare rates of nosocomial pneumonia between gastric and jejunal fed patients as measured by: a) new & persistent infiltrate on chest x-ray (CXR), b) fever, c) sputum culture, d) leukocytosis, and e) bronchoscopically directed protected specimen brush. 3) To compare colonization rates between a subset of gastric and jejunal fed patients, at three sites (oropharynx, trachea, stomach); specific focus being Gram-negative bacilli, as measured by quantitative and qualitative microbiology analysis.

**Technical Approach:** Shortly after having a feeding tube placed, the principal investigator or the project director will conduct a noninvasive metabolic test at the bedside to estimate calorie needs for tube feeding. This test measures the amount of energy used by a patient while ill in the ICU. It will be performed each week. In addition, specimens of blood, urine, sputum and stomach contents will be obtained to evaluate nutritional status and monitor for infection or bleeding. Lastly, the health record will be examined by the investigator or the project director for the following information: pertinent medical history, admission vital signs, current medications, height and weight, and tube feeding regimen.

**Progress:** A total of 53 adult critically ill subjects were recruited; of this 49 were included in the study with 4 subjects which were never fed and were excluded from data analysis. There were no significant differences between groups for any variable measured upon entry into the study. In general the study population was comprised of elderly subjects with a high score for severity of illness (APACHE II >20) suggestive of many contributing comorbid conditions. The high number of ventilator days (mean = 10.2 days) and increased length of hospital stay (mean = 19.9 days) also reflect the acuity of their medical condition. There was no difference in nutritional status at randomization for subjects in either the gastric group or the jejunal group. Both albumin and prealbumin levels were severely depressed upon randomization. However, measured serum albumin values for Day 5 of feeding reflect significantly higher value for the jejunal group. Chi-Square analysis of GI symptom distress demonstrated a statistically significant ( $p < 0.05$ ) difference in abdominal distention between the two groups. The jejunal feeding group experienced more abdominal distention in the first week of feeding than the gastric group. This study revealed no significant differences between groups in number of days fed, calories received per day, percent daily goal caloric intake, or residual volumes. By day 3, both groups had achieved only 70% of their daily caloric goal intake. Rates of nosocomial pneumonia were high in the general study population (41%), and by assigned group (Gastric = 39.4%, Jejunal = 50%). However, Fischer's Exact Test revealed no significant difference between groups ( $p = 0.345$ ). Contrary to other scientific findings, this study did not confirm that jejunal feeding affords additional benefits in terms of greater improvement in nutritional markers and increased caloric intake when compared to gastric feeding. In addition, both groups experienced frequent bouts of gastrointestinal symptom distress. The lack of difference in outcomes between groups and the high rates of pneumonia and mortality suggest that all therapies require careful consideration of risk versus benefit.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/063	<b>Status:</b> Ongoing
<b>Title:</b> Improving ALI/ARDS Patient Outcomes with Metabolic Support		
<b>Principal Investigator:</b> MAJ Mary S. McCarthy, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Maginia S. Morales, AN; Janet C. Chilton		
<b>Start Date:</b> 3/20/1998	<b>Est. Completion Date:</b> Sep 00	<b>Periodic Review:</b> 2/22/2000

**Study Objective:** 1) What are the differences in nutritional and physiologic responses between ARDS patients who receive a special formula (Oxepa) versus ARDS patients who receive a standard formula (Osmolite HN)? (2) What are the differences in patient outcomes between ARDS patients who receive a special formula (Oxepa) versus ARDS patients who receive a standard formula (Osmolite HN)?

**Technical Approach:** Subjects will be randomized to receive either immune-enhanced formula (Oxepa) or a standard stress formula (Osmolite HN) for a minimum of 4 days. Nutritional outcomes will be based on prealbumin values, nitrogen balance, and % caloric goal achieved. Physiologic outcomes will be measured by the oxygenation ratio respiratory quotient, and plasma interleukin-6 levels.

**Progress:** 7 subjects were enrolled in FY00, for a total of 13 subjects enrolled at MAMC. Subject enrollment continues through June 2001.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/041	<b>Status:</b> Completed
<b>Title:</b> Knowledge Retention in Advanced Cardiac Life Support Trained Registered Nurses Using American Heart Association Standards for Care During the First 10 Minutes of a Cardiac Arrest		
<b>Principal Investigator:</b> MAJ Penny M. Moureau, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LCDR Kathy W. Bay, USN		
<b>Start Date:</b> 2/22/2000	<b>Est. Completion Date:</b> Mar 00	<b>Periodic Review:</b> N/A

**Study Objective:** (1) Determine if the subjects can effectively prioritize activities for the first 10 minutes of a resuscitation attempt, (2) Determine if the subjects can correctly identify common lethal arrhythmias, (3) Determine if the resuscitation attempt of a patient in cardiopulmonary arrest follows American Heart Association (AHA) guidelines, (4) Relate knowledge level to length of time since ACLS training (5) Identify if the nurses are aware of their practice facility's policy regarding the use of the defibrillator.

**Technical Approach:** This study will administer questionnaires to ACLS trained nurses which will test their retention of knowledge since they were last trained in Advanced Cardiac Life Support.

**Progress:** This study has been fully implemented with 828 questionnaires sent out and 309 usable questionnaires returned. Retention rates of ACLS knowledge was shown to be 90% for nurses who had trained in the last 6 months. Rates dropped to 88% one year after training, and 82% two years after training. Over 90% of the nurses correctly identified six common lethal arrhythmias.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/067

**Status:** Ongoing

**Title:** Weight and Body Fat Percentage Gain or Loss at ROTC Advanced Camp 2000

**Principal Investigator:** LTC Joan K. Vanderlaan, AN

**Department:** Nursing

**Facility:** MAMC

**Associate Investigator(s):** CPT Nicole L. Kerkenbush, AN; CPT Corina Barrow, AN

**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Nov 00

**Periodic Review:**  
N/A

**Study Objective:** To answer the following questions: (1) Do Cadets lose or gain weight at camp? (2) If so, how much weight (in lbs.) do they gain or lose? (3) Are there gender and racial variables to the weight change? (4) If weight loss does occur, is there a difference between Cadets who are trying to lose weight versus those who don't care about weight loss? (5) Does the weight loss affect tape results utilizing the Army system? That is, can weight loss be correlated to change in % body fat? and (6) If Cadets are minimally overweight or overtape at the beginning of camp, would they lose enough weight or % body fat during camp to justify the time and expense of retaining them at camp as a means of improving ROTC officer commission production?

**Technical Approach:** Cadets will be informed of the purpose and procedures of the study and given the option to participate or not. During the commissioning physical, they will answer a brief questionnaire and their height and weight will be recorded as per Army APFT standards. For one platoon per Regiment, consenting cadets will also be taped according to the Army taping procedure as described in AR 600-9. This occurs on day 2 of the 35 day camp cycle. On day 34 of the camp cycle, cadets will again be weighed and those previously taped will be taped again.

**Progress:** 3,195 subjects enrolled and data collected. Preliminary data analysis shows that males as a group decreased body fat percentages during camp. Body fat gain/loss for females has not yet been established. Further data analysis is being conducted. Further subject enrollment is not planned at this time.

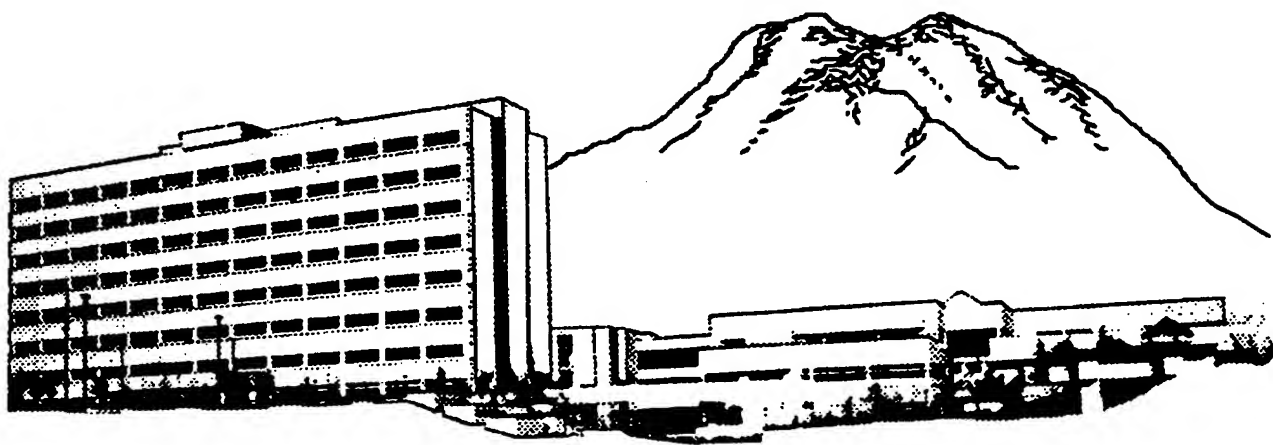
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/028	<b>Status:</b> Completed
<b>Title:</b> Self-efficacy for Exercise and the Perceived Barriers and Benefits of Exercise Among Pregnant Soldiers		
<b>Principal Investigator:</b> Larry Whorley, RN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Lori L. Trego, AN; CPT Robin O'Dell, AN		
<b>Start Date:</b> 2/22/2000	<b>Est. Completion Date:</b> Feb 00	<b>Periodic Review:</b> N/A

**Study Objective:** To describe pregnant soldiers' perceived self-efficacy for performing exercise and their self-defined benefits and barriers to performing exercise during pregnancy.

**Technical Approach:** Consenting active-duty military women will be asked to complete questionnaires during the New OB Registration class or at a prenatal visit.

**Progress:** This study completed subject enrollment 10 Jul 00 at MAMC. 40 active-duty women completed the surveys. Results indicate that those who perceived benefits to exercise had a higher self-efficacy and those who perceived barriers to exercise had a lower self-efficacy for performing exercise during pregnancy. Findings suggest that the more the women believe that performance of exercise during pregnancy will produce positive effects on their physical health status, the more they believe that they can perform exercise during pregnancy. Results also revealed the importance of recognizing the psychological factors that affect exercise behavior. Self-efficacy may in turn influence performance of exercise behavior.



## Detail Summary Sheets

Anesthesia Students,  
Department of Nursing

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/006	<b>Status:</b> Completed
<b>Title:</b> The Effect of Positioning During Administration of 0.5% Isobaric Bupivacaine on Sensory Level Block		
<b>Principal Investigator:</b> CPT Christopher Domer, AN		
<b>Department:</b> Nursing/Anesthesia	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Ann-Marie Starr, AN; 1LT Charles Eric Ritter, AN		
<b>Start Date:</b> 10/26/1999	<b>Est. Completion Date:</b> Sep 00	<b>Periodic Review:</b> N/A

**Study Objective:** The purpose of this study is to examine the effect of position on the subsequent height of sensory block achieved following administration of an isobaric anesthetic into the subarachnoid space.

**Technical Approach:** The study enroll 42 subjects scheduled for elective lower extremity surgery. Neither the researcher nor the patient will be blinded to which group the patient is assigned because position during administration will be manipulated. Subjects will be randomly divided to one of three groups. Group 1 subjects will receive the spinal anesthetic solution in the lateral decubitus and turned supine. Group 2 subjects will be seated during injection and placed supine. Group 3 subjects will be seated during injection and remain in the seated position for 2.5 minutes before being placed supine. Each study subject will receive 4 ml (20 mg) of 0.5% isobaric bupivacaine. The investigator administering the subarachnoid anesthetic will record the sensory level block 5, 10, 15 and 30 minutes after administration of the subarachnoid block.

**Progress:** The initial pilot with 6 subjects was successful; therefore, a change of study methods was deemed necessary. The study was reported completed, 14 Aug 00. Sample size consisted of 30 patients between the ages of 18 and 65 scheduled for elective lower extremity surgery. Analysis of data showed no clinical difference in mean height of sensory blockade based on patient position during and after administration of the spinal anesthetic.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/135

**Status:** Ongoing

**Title:** A Comparison in the Early Reversal of Rapacuronium with Neostigmine and Edrophonium

**Principal Investigator:** CPT Brock M. Smith, AN

**Department:** Nursing/Anesthesia

**Facility:** MAMC

**Associate Investigator(s):** CPT Charles T. Lent, AN; CPT Daniel R. Mattson, AN; CPT Kyle E. Ewing, AN; CPT Paul M. Johnson, AN

**Start Date:**  
9/26/2000

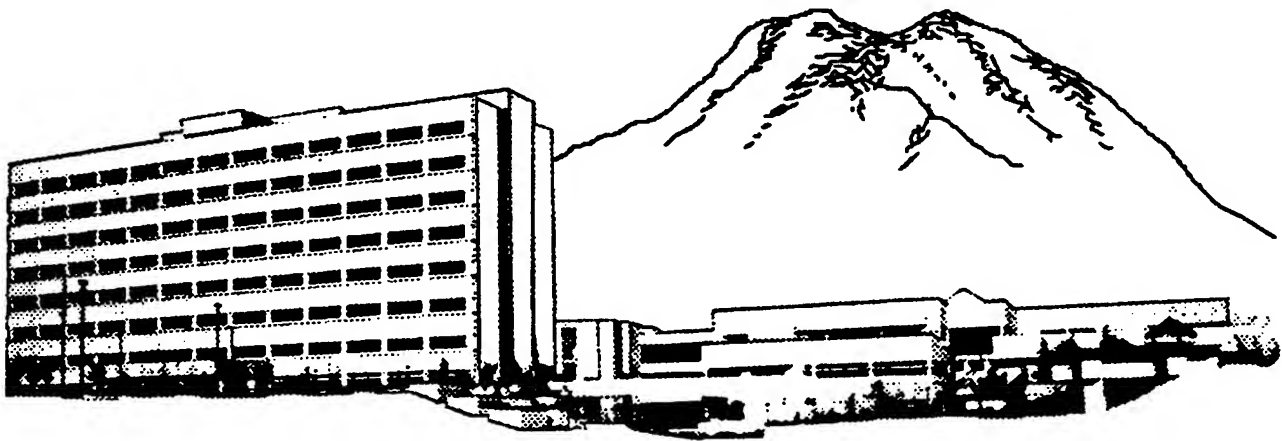
**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
N/A

**Study Objective:** The purpose of this study is to determine whether endrophonium or neostigmine produces a faster return of the trail-of-four (TOF) ratio to 0.7 following an intubating dose of rapacuronium.

**Technical Approach:** The purpose of this double-blind, randomized, Phase IV drug study is to determine the fastest means of reversing rapacuronium. A convenience sample size of 100 subjects undergoing general anesthesia for surgery will be used. Subjects will be randomized to receive either neostigmine 0.07 mg/kg with glycopyrrolate 0.01 mg/kg diluted with 0.9% sodium chloride solution or endrophonium 1.0 mg/kg with atropine 0.01mg/kg diluted with 0.9% sodium chloride. Following the reversal of rapacuronium data will be collected on onset, recovery of T1 to 25% and 75%, TOF ratios of 0.7 and 0.8.

**Progress:** This protocol recently received review and approval by the IRB, but has not yet received final approval to begin subject enrollment at MAMC.



## Detail Summary Sheets

### Nutrition Care Division



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/132	<b>Status:</b> Ongoing
<b>Title:</b> Army Weight Control Program - Identifying Predictors of Success			
<b>Principal Investigator:</b> CPT Michelle D'Amico, SP			
<b>Department:</b> Nutrition Care			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> 2LT Hillary Harper, SP			
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> Jun 01		<b>Periodic Review:</b> N/A

**Study Objective:** The aims of this study are to (1) identify factors that predict the ability of Active Duty soldiers in the AWCP to successfully achieve the standards and (2) specifically, identify the motivators, attitudes and practice behaviors related to successful achievement of AWCP standards.

**Technical Approach:** Soldiers enrolled in the Active Duty Weight Control Program, Fort Lewis, WA, will complete an initial and 6 month follow-up questionnaire. Questionnaires will be anonymous and information will be reported in aggregate form only with no participant identifiers.

**Progress:** This protocol recently received review and approval by the IRB. No work has been initiated on this study in FY 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/082	<b>Status:</b> Completed
<b>Title:</b> Implementation and Evaluation of PEP (Personal Energy Plan) Health and Wellness Program Designed to Promote Healthy Eating and Physical Activity Among Adult Participants		
<b>Principal Investigator:</b> CPT Michelle D'Amico, SP		
<b>Department:</b> Nutrition Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> JC Hare; S Hite; L Kostner; J Spahn; P Jones; R Cavalcanti; M Perious; LTC Linda L. Rowbotham, SP		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Mar 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if the implementation of CDC's PEP Program will make a difference in healthy eating and physical activity knowledge and behaviors within DoD and to determine the factors (e.g., gender, beneficiary status, stage of readiness, rank, education level, type of worksite environment) that best predict whether or not an individual will experience a positive change in physical activity or eating.

**Technical Approach:** Study design is quasi-experimental, one group pre- and post-evaluation. Squadrons/units will be selected as potential sites for intervention. Site coordinator will meet with the commander and explain program and identify the amount of unit time that will be required to participate along with the expected benefits. Once commander's approval is obtained, the worksite audits must be done at either flight level prior to beginning the recruitment of participants. (Questionnaire will need to be identified as to what is "installation level" versus likely to change at flight to save evaluator time.) The PEP program consists of a promotional phase lasting approximately 8 weeks during which the program is marketed to recruit participants and a 12-week implementation phase. Participants that indicate an interest will be provided with an enrollment packet consisting of the informed consent form and PEP enrollment forms. The PEP enrollment forms will be analyzed to determine stage of change and registration log will be completed which assigns each participant an identification number (to maintain confidentiality). Only the on-site researcher will have access to the log with personal identification and identification numbers. Personal identification numbers will also be assigned to control group. Pretests will be distributed to all enrolled participants as well as control group from another worksite with similar composition. Instructions encouraging partners will be provided with the pretest. After all pretests are collected, partners will be assigned, kits will be distributed and dates recorded when each kit was provided to participant. Each month following the first month, a new calendar will need to be distributed to the participants. A telephone call will be made to all participants weekly to see how they are progressing and answer any questions about the PEP program. The telephone call will ask the participants to identify which part of the materials they have reviewed, provide encouragement for completing the next steps as outlined in the materials, ensure that they do not need additional program materials, and answer any questions that they may have

Variables that will be assessed in the current study include physical activity stage, healthy eating stage, amount of physical activity, nutritional intake level, health knowledge, perceived energy, attitudes toward physical activity, attitudes toward healthy eating, environmental support, and worksite supportiveness. Participants will be classified according to their physical activity stage and healthy eating stage based on their: responses to the initial questionnaire (e.g., Precontemplation Stage, Preparation Stage, Late Preparation Stage; see description above); amount of physical activity, nutritional intake level, health knowledge, perceived energy score, attitudes toward physical activity score, attitudes toward healthy eating score, environmental support score, worksite supportiveness score (based on the outcome of the worksite audit for his/her facility)

Descriptive statistics/frequencies for each of the major outcome variables will be tabulated. Statistics will be calculated separately for each of the two assessment points (pre- and post-PEP intervention). Pre- and post-intervention scores for each of the major outcome variables will be compared using a series of Wilcoxon-signed-rank tests. Logistic regression will be used to assess the factors that predict whether or not an individual will experience a positive change in stage after participating in the PEP program (e.g., going from the Contemplation Stage to the Preparation Stage). Independent variables that will be included in the model will be gender, age, beneficiary status, Pre-intervention Stage, and supportiveness of worksite environment. Separate models will be conducted for physical activity stage and healthy eating stage.

**Progress:** Fort Lewis was one site in this multicenter study conducted by DoD. Participants were administered pre- and post-tests over a twelve week period, in addition to self-paced, self-administered worksheets from two workbooks. Data collection has been completed; however, no results or conclusions have been made at the time of this report. Data analysis is in progress by the Cooper Institute for aerobics Research.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 99/111

Status: Ongoing

Title: An Evaluation of UPBEAT Weight Management Program

Principal Investigator: 1LT Joseph T Frost

Department: Nutrition Care

Facility: MAMC

Associate Investigator(s): 1LT Susan Ann Jordan, SP

Start Date:  
9/28/1999

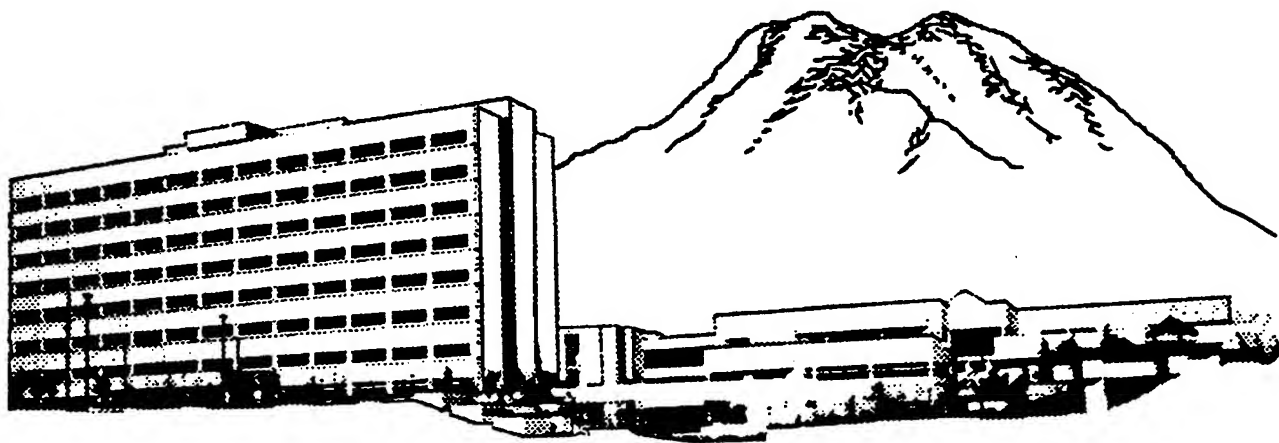
Est. Completion Date:  
Nov 99

Periodic Review:  
11/28/2000

**Study Objective:** (1) To educate soldiers about the mind and body drives that lead to overeating and inactivity, (2) To increase soldier readiness through sustained improvement in overall health and fitness, and (3) To decrease losses in personnel due to AR 600-9.

**Technical Approach:** UPBEAT Program will consist of 4 phases: orientation/testing, personal interviews, Skill Training, Partnering for Change, and Maintenance and Relapse Prevention. This first phase will assess the soldiers' readiness to change, and develop individualized goals and outcomes. This phase will also identify if a soldier has an eating disorder. Based on the efforts of phase 1, the second phase will involve commanders and UPBEAT staff partnering for soldier success. The third phase will involve a 12- week intervention aimed at identifying the mind and body cues that will lead to permanent lifestyle changes and improved overall health. The fourth phase will focus on the maintenance of these skills and behaviors. This phase is essential in working through any relapses and is considered crucial in long term success. This phase will extend out to a full year.

**Progress:** 46 subjects were enrolled onto this protocol during FY00. Final data analysis is not yet available. Subject enrollment continues.



## **Detail Summary Sheets**

Department of Obstetrics/Gynecology

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/068      **Status:** Ongoing

**Title:** The Role of Methergine in the Management of Spontaneous Abortion

**Principal Investigator:** CPT Jodi L. Bergemann, MC

**Department:** OB/GYN      **Facility:** MAMC

**Associate Investigator(s):** LTC Gregory E. Chow, MC

**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** 1. Comparison of failure rates of conservative therapy in management of spontaneous abortions. Failed conservative management is defined as requiring a dilation and curettage

2. Amount of blood loss

3. Duration to completion of spontaneous loss (# days until quantitative BHCG<5)

4. Pain scale (control vs. methergine)

**Technical Approach:** Patients presenting with the clinical and laboratory diagnosis of spontaneous abortion and desiring conservative therapy will be randomized to methergine or placebo treated groups. Each group will be asked to take their medication for 24 hours. On Day #1, laboratory data including CBC and quantitative B-HCG will be obtained. B-HCG values will be followed on Days #4 and #7, then weekly until values are below 5 (indicating uterine evacuation). At this time, a CBC will be evaluated and the patient will complete a pain scale to measure amount of pain associated with the treatment.

**Progress:** This protocol has not begun enrollment of patients at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/031	<b>Status:</b> Ongoing
<b>Title:</b> Relationship of Cesarean Delivery for Arrest of Descent and Station at Onset of Maternal Pushing: A Case Control Study		
<b>Principal Investigator:</b> CPT Richard O. Burney, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> C Frayer; Sylvia Wood, RN; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC		
<b>Start Date:</b> 2/23/1999	<b>Est. Completion Date:</b> Apr 99	<b>Periodic Review:</b> 2/22/2000

**Study Objective:** To determine the effect of station at onset of second stage on the rate of cesarean delivery in primiparous patients with epidural anesthesia.

**Technical Approach:** Using the 1996/1997 labor and delivery records of deliveries at MAMC, a case control study will be performed. All primiparous patients with epidural anesthesia who required a cesarean section for arrest of descent will be identified and labeled as cases. For each case, two primiparous patients with epidural anesthesia who progressed to spontaneous delivery will be identified and labeled as controls. For each case, respective controls will be matched for maternal age, gestational age, fetal weight and use of oxytocin in labor. During this period of labor management, all patients began pushing efforts at the onset of the second stage, which was defined as cervical progression to complete effacement and complete dilation irrespective of fetal station. The fetal station at the onset of second stage will be determined for all cases and controls

A chi-square analysis will be performed to compare cases and controls with second stage maternal pushing efforts begun at fetal station 0 and higher. This will be conducted so as to allow the determination of an odds ratio for operative delivery when maternal pushing efforts are begun at fetal station higher or equal to 0. Additionally, each station will be assigned a value to allow for the performance of the Mann-Whitney Rank Sum Test in the comparison of cases and matched controls.

**Progress:** 30 records have been reviewed during FY00. No findings/conclusions have been drawn to this point. Record review continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/130	<b>Status:</b> Completed
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**Title:** Use of OSATS (Objective Structured Assessment of Technical Skills) to Objectively Assess Surgical Competence

**Principal Investigator:** LTC Gregory E. Chow, MC

**Department:** OB/GYN

**Facility:** MAMC

**Associate Investigator(s):** CPT Robert W. Chalmers, MC; LTC Peter E. Nielsen, MC

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
N/A

**Study Objective:** Objectively measure surgical skills and task oriented competency using OSATS with blinded, independent evaluators and determine interobserver reliability of the OSATS as an assessment tool by comparing the evaluations of those blinded to each resident year level to those not blinded.

**Technical Approach:** This is a prospective cohort study on the performance of 7 predetermined tasks by residents with objective evaluation of each procedure performed by 3 faculty, one of which will be blinded to resident year level and the other two that will not be.

**Progress:** Work on this study has been reported as completed. Evaluation of surgical skills was performed, 27 Sep 00, on 16 residents from MAMC at 7 skill stations and evaluated (1 from UW and at least 1 from MAMC). All data has been collected and data analysis is in progress.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/106	<b>Status:</b> Ongoing
<b>Title:</b> Tubal sterilization with the Ligasure vessel sealing system		
<b>Principal Investigator:</b> CPT Lisa M. Foglia, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Louis A. Dainty, MC; LTC Peter E. Nielsen, MC; COL Milo L. Hibbert, MC; CPT Ruth A Reardon, MC		
<b>Start Date:</b> 6/27/2000	<b>Est. Completion Date:</b> Sep 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether the Ligasure Vessel Sealing System may be used to effectively seal fallopian tubes as evidenced by gross and histological examination.

**Technical Approach:** Subjects will have a preoperative evaluation that will include obtaining a history, physical examination, preoperative anesthesia visit, and laboratory studies (CBC, hCG). Subjects will be randomized on a 1:1:1 basis to three different treatment groups - 1 seal per Fallopian tube, 2 seals per Fallopian tube, 3 seals per Fallopian tube with the Ligasure device. A laparoscopic tubal ligation will be performed. A mid-isthmus segment of the right Fallopian tube will be identified. The Ligasure device will be inserted through the suprapubic port, and a mid-isthmus segment of Fallopian tube will be grasped with the Ligasure device. It will be sealed one, two or three times depending upon which group the patient was assigned to. The Ligasure device will be removed and then a laparoscopic Pomeroy will be performed where the ligated segment of tube is excised and removed. The length of the tubal segment removed will not be altered by the Ligasure procedure.

The segments of Fallopian tube will be submitted to Pathology, as per usual for the Pomeroy procedure. The tubal diameter (lumen and external diameter), length of tubal occlusion, and length of tissue damage beyond the length of tubal occlusion will be measured in millimeters. The tubal segments will be examined histologically for extent of spread of tissue damage. Presence or absence of tubal occlusion will be determined by ability to cannulate the tubes with a lacrimal duct probe and then by histologic examination of the tube. The presence/absence of tubal occlusion will be compared by group. The length of tubal occlusion and length of tissue damage beyond the length of tubal occlusion will be compared by group, using the ANOVA.

**Progress:** This study recently received final IRB approval. No work has been initiated on this study in FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/129	<b>Status:</b> Ongoing
<b>Title:</b> An Introductory Training Program for New PGY-1, PGY-2, and PGY-3 Obstetrics & Gynecology Residents			
<b>Principal Investigator:</b> CPT Robert H. G. Holland, MC			
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Lisa M. Foglia, MC; LTC Peter E. Nielsen, MC			
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> Aug 01		<b>Periodic Review:</b> N/A

**Study Objective:** Demonstrate that an initial training process improves the performance and knowledge base of new interns and residents.

**Technical Approach:** This is an educational intervention study. A series of 20 minute lectures and/or demonstrations on basic obstetric , gynecologic, and infertility topics will be given to all new PGY-1 and PGY-2 residents, with curriculum pretest, immediate posttest, delayed posttest and a qualitative survey on performance, confidence and competence. Pretests and posttest results will be compared and evaluations will be compared to determine both subjectively and objectively whether this training appears to benefit this group of residents.

**Progress:** Initial educational intervention and quiz done; comparisons and evaluations continue. All that remains to be completed is the posttest.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/001

**Status:** Completed

**Title:** Female Soldier Readiness: A Leader's Guide-Implementation Phase: Utility Validation Survey

**Principal Investigator:** LTC Peter E. Nielsen, MC

**Department:** OB/GYN

**Facility:** MAMC

**Associate Investigator(s):** CPT David J. Phillips, MS; COL Roderick F. Hume, MC; CPT Tiffany Vara, MSC; COL Jeffrey D. Gunzenhauser, MC; MAJ Diane M. Flynn, MC; COL Robert E. Ricks, MC; LTC Byron C. Calhoun, MC, USAF; COL Paul Whittaker, MC; LTC Wilma Larsen, MC; MAJ Mary Jo Laurin, SP; CPT John Barrett, MC; CPT Mayelien Shipman, MSC

**Start Date:**  
10/26/1999

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
N/A

**Study Objective:** To evaluate the utility of our ongoing initiative for Female Soldier Readiness by developing a handbook for small unit leaders to facilitate optimal personnel management for female soldiers. The current study will seek to determine at what level and to which personnel components, and when in a career would integration of the handbook be best (military schools).

**Technical Approach:** Handbooks will be distributed during unit leadership training coordinated through the I Corps Surgeon and the Fort Lewis Units. A program of education intervention will be followed with outcome variables of satisfaction and optimization of the guide through formal and informal focus group feedback. Units selected will receive a briefing and distribution of handbook. The second visit will include review of feedback, administration of survey tool and focus group discussion.

**Progress:** This protocol has collected reviews from 159 participants during FY00. The project has been completed. Results from this protocol demonstrate a clear approval of the guide as a useful tool for leaders at the platoon level with training implemented at the Officer Basic and Primary Leadership Development courses.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/023

**Status:** Ongoing

**Title:** Delayed Maternal Pushing with Labor Epidural Analgesia: Effects on Operative Vaginal Delivery

**Principal Investigator:** LTC Peter E. Nielsen, MC

**Department:** OB/GYN

**Facility:** MAMC

**Associate Investigator(s):** CPT Richard O. Burney, MC; MAJ Brian T. Pierce, MC; MAJ Christina Apodaca, MC; MAJ Richard K. Wagner, MC; Sylvia Wood, RN; Thomas W. Overly; LTC Byron C. Calhoun, MC, USAF; Kathleen M. Judge; CPT Robert W. Chalmers, MC

**Start Date:**  
1/26/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
3/28/2000

**Study Objective:** To determine the effect of delayed maternal pushing on the rate of operative vaginal delivery.

**Technical Approach:** Following consent, subjects will continue to be managed according to standard of care. When study eligibility criteria is met, subjects will be randomized into one of two treatment groups after the placement of epidural analgesia; early pushing and delayed pushing.

**Early pushing group:** Subjects will be allowed to push at the first maternal urge once the cervix is completely dilated.

**Delayed pushing group:** Subjects will begin pushing when the vertex is distending the perineum. The subjects in this group will be given 0.25% bupivacaine epidural boluses to delay the maternal urge to push.

Cervical examinations in both groups will occur at either maternal urge to push, or at 2 hours following complete cervical dilation. If no maternal urge to push at 2 hours, and the descent of the vertex is  $> 1$  cm/hr, then continue management as randomized. If descent  $< 1$  cm/hr, then begin oxytocin infusion per protocol for hypo tonic contractions and reexamine cervix in 2 hours, or at the onset of urge to push. If uterine activity is adequate, then begin pushing in both groups. Reexamine cervix in 2 hours and evaluate for arrest of descent. This management may allow the length of the second stage to be extended to approximately 5 hours, exceeding the generally accepted length of 3 hours in nulliparas and 3 hours in multiparas with epidural analgesia. The type of operative intervention (forceps, vacuum or cesarean delivery) will be the decision of the attending physician to ensure a safe and effective delivery.

**Progress:** 33 subjects were enrolled in this study in FY00, for a total of 49 subjects enrolled at MAMC. Subject enrollment is ongoing. No conclusions or findings are available at this time.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/024

**Status:** Ongoing

**Title:** Extending the Duration of Active Phase Arrest: Effects on Cesarean Delivery

**Principal Investigator:** LTC Peter E. Nielsen, MC

**Department:** OB/GYN

**Facility:** MAMC

**Associate Investigator(s):** CPT Amy J. Asato, MC; MAJ Brian T. Pierce, MC; MAJ Christina Apodaca, MC; MAJ Richard K. Wagner, MC; Thomas W. Overly; LTC Byron C. Calhoun, MC, USAF

**Start Date:**  
1/26/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
4/25/2000

**Study Objective:** To determine the effect of extending the length of active phase arrest of dilation from 2 to 4 hours on the rate of cesarean delivery.

**Technical Approach:** Following consent, subjects will continue to be managed according to standard of care. When study eligibility criteria is met, subjects with active phase arrest, despite 2 hours of adequate uterine activity and continuous labor epidural analgesia, will be randomized to either cesarean delivery or 2 additional hours of labor. All subjects at the end of this 2 hour study period who fail to demonstrate cervical change ( $< 1$  cm progress in 2 hours) will be delivered by cesarean section. All other patients will continue the labor process. Cesarean delivery for non reassuring fetal heart rate tracing will be performed based on routine obstetric indications.

**Progress:** 6 subjects have been enrolled in FY00, for a total of seven subjects enrolled in this study at MAMC. Subject enrollment is ongoing. No data analysis or conclusions are available at this time.

### Detail Summary Sheet

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<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/046	<b>Status:</b> Ongoing
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**Title:** Outcome of Infants Born at 22-28 Weeks Gestation: A Retrospective Review in Military Care Facilities

**Principal Investigator:** LTC Peter E. Nielsen, MC

**Department:** OB/GYN

**Facility:** MAMC

**Associate Investigator(s):** LTC Michael K. Yancey, MC; LTC Gary C. Sharpe, MC, USAF; MAJ Peter G. Napolitano, MC; MAJ Wanda A. Barfield, MC; MAJ Gregory A. Marindovich, MC; MAJ Christina Apodaca, MC; MAJ Richard K. Wagner, MC; LTC Byron C. Calhoun, MC, USAF; MAJ Brian T. Pierce, MC

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**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
3/28/2000

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**Study Objective:** To analyze and report neonatal morbidity and mortality in early gestation in military care facilities.

**Technical Approach:** All neonates born between 22 and 28 weeks EGA, inclusive, will be identified through hospital coding systems. A chart review will be performed on both the mother and neonate. Data will be collected to include: Gestational age at delivery, delivery weight antepartum betamethasone administration, neonatal surfactant administration, maternal age and race, and specific neonatal complications to include: death, RDS, WH (grade 3 and 4), periventricular leukomalacia, NEC, hyperbilirubinemia requiring phototherapy or exchange transfusion, retinopathy of prematurity, hypoglycemia, and sepsis. Maternal medical problems and ante/intrapartum complications will also be recorded. A follow-up study is planned to report long term follow up in these premature infants, specifically at 2 years of age and 5 years of age. The data will be collected on a separate data sheet (attached), with the patient being identified by a code number. The principle investigator will be the sole keeper of the names of the patients as well as the code to which they are assigned.

**Progress:** No data has been collected at this time. Anticipated date for initial data collection is January 2001.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/084

**Status:** Ongoing

**Title:** Team Performance in Labor & Delivery: L&D MedTeams: Concept Phase

**Principal Investigator:** LTC Peter E. Nielsen, MC

**Department:** OB/GYN

**Facility:** MAMC

**Associate Investigator(s):** COL Matthew M. Rice, MC; COL Romeo P. Perez, MC; LTC Byron C. Calhoun, MC, USAF; Kathleen M. Judge; Robert Simon, EdD; COL Roderick F. Hume, MC

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
11/28/2000

**Study Objective:** The proposed study, Concept Phase, is intended to develop an educational initiative in teamwork training (MedTeams) for Labor Delivery. Observational Study to determine components of curriculum and optimal training curriculum. Culmination in Experimental Phase pending successful Grant Application FY2000.

**Technical Approach:** This study is intended to demonstrate that an educational initiative in teamwork training (MedTeams) can be instrumental in improving labor & delivery caregiver performance and job satisfaction while reducing error patterns that are potentially dangerous to patients, mother and child. This initiative has its beginnings in the aviation community through team coordination training entitled "Cockpit Resource Management". Cockpit Resource Management in essence are rules of engagement that crew members abide by when communicating with one another, (i.e., check back, challenge, etc). This simple innovation was found to be a powerful one within the last several years and has contributed to a decrease in both civilian and military aviation mishaps. The successful multicenter educational trial involving the ETCC has proven that a similar initiative in medicine can reduce medication errors and other actions that are potentially harmful to patients. MedTeams has been funded by DA through ARL under a MOA with DRC and collaborating Medical Centers to test this hypothesis in emergency departments. A suite of both objective and subjective measures will be developed at MAMC under this expedited review protocol to pilot an L&D MedTeam educational initiative at MAMC. This program will serve as the core for the next phase, experimental phase, of a multicenter educational interventional trial which will parallel the ETCC trial. The Program will involve an eight-hour MedTeams didactic training, frequent refresher and reinforcement sessions, in addition to the administration of anonymous caregiver and patient survey tools. Commonly available continuing improvement and risk management data will be monitored to follow trends of error patterns, medication error, patient complaints, etc. Goal to develop Grant Proposal and Multicenter Trial by Oct 2000. CRDA with DRC, MAMC/CIRO through Geneva will develop concurrently.

**Progress:** 19 charts have been identified and are being review by physician/nurse teams to determine whether teamwork failure may have contributed to particular clinical outcomes. Retrospective chart review is ongoing.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/077		<b>Status:</b> Ongoing	
<b>Title:</b> Misoprostol for the Medical Management of Non-viable First Trimester Pregnancies					
<b>Principal Investigator:</b> CPT Jason D. Parker, MC					
<b>Department:</b> OB/GYN				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Milo L. Hibbert, MC; LTC Peter E. Nielsen, MC; Troy H. Patience, B.S.; CPT Louis A. Dainty, MC					
<b>Start Date:</b> 6/22/1999		<b>Est. Completion Date:</b> Mar 01		<b>Periodic Review:</b> 3/28/2000	

**Study Objective:** The purpose of this study is to examine the effectiveness of misoprostol (Cytotec; GD Searle and Co., Chicago, IL) for the management of non-viable first trimester pregnancies. Specifically, misoprostol (15-S-15-methyl PGE1) will be compared to a placebo with expectant management in who have documented non-viable gestations. We will examine the following outcome variables: time to resolution, number of patients requiring dilation and curettage, change in hematocrit, cost to the institution, patient satisfaction, and reported side effects.

**Technical Approach:** Patients presenting to the OB/GYN clinic with a nonviable gestation will be considered potentially eligible to participate in the study. The diagnosis of non-viable gestation will be documented by endovaginal ultrasound. Those patients entering the study will be directed to the OB/GYN clinic for evaluation, exam, counseling and to watch the video giving explanation of purpose of the study and the planned procedure, but also expected side effects and possible complications. An anembryonic gestation will be diagnosed in any patient with an irregularly shaped gestational sac and mean sac diameter of 16 or greater without an embryonic pole. Additionally any patient with an intrauterine fetal pole between 5 and 14 mm with no cardiac activity will be considered non-viable and will be considered for acceptance into our study. Ultrasonic findings will be verified by two of the resident staff from the obstetrics and gynecology department of Madigan Army Medical Center. After explanation of the study, verification that the patients meet the inclusion criteria, patients will be offered participation in the study and asked to view a short video to ensure consistency of counseling. Upon conclusion of the counseling and video, patients will be asked to sign a consent form for participation in the study.

Complete history and physical will be performed and initial laboratory will be obtained to include CBC, BUN, creatinine, quantitative BHCG and blood type to include Rh status. Patients will then be randomized into two groups: study group receiving misoprostol per vagina and the control group receiving a placebo per vagina.

Subjects will be issued an envelope and asked to report to the pharmacy where they will pick up their study medication, which will be blinded to them and the provider administering the medication. Additionally, they will be given Motrin and Phenergan to help alleviate undesired side effects. Subjects will have four 200 ug tablets of misoprostol in the posterior fornix of the vagina using a speculum under the direct visualization of the provider.

Patients will be asked to return in 24 hours for re-examination to include a pelvic ultrasound using a vaginal probe. If no evidence of an intrauterine pregnancy remains (i.e. gestational sac, fetal pole etc.), patients will be informed that their miscarriage was complete, given precautions and asked to make an appointment for follow-up in 4 weeks in addition to weekly visits to the lab for quantitative BHCG. All patients will be followed until the quantitative BHCG has fallen zero to ensure resolution of the pregnancy event.

Those patients with evidence of a gestational sac will be given a second dose of misoprostol or alternatively a D&C if they choose to withdraw from the study or surgical intervention is deemed clinically indicated by the attending staff. Again, the subjects will be given appropriate



counseling and precautions and asked to follow up in an additional 24 hours for re-evaluation. At any point in the study, subjects may withdraw from the study as per the patient's wishes or removed from the study if the provider feels surgical intervention is indicated (i.e. excessive bleeding or side effects). Surveys will be given at each visit and follow up to evaluate patient satisfaction and also to query for unintended side effects and complications.

**Progress:** 6 patients have been enrolled onto this ongoing protocol. No conclusions or outcomes have been found to date. Enrollment will continue until the target 30 subjects are enrolled.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/127      **Status:** Ongoing

**Title:** Mentoring for the New Millennium: Enhanced Scholarly Activity, Professional Development, and Personal Satisfaction for Future Academics Through the Successful Implementation of a Mentor System

**Principal Investigator:** COL Robert E. Ricks, MC

**Department:** OB/GYN      **Facility:** MAMC

**Associate Investigator(s):** COL William O. Walker, Jr., MC; COL Patrick C. Kelly, MC; LTC Peter E. Nielsen, MC; LTC Gregory E. Chow, MC; LTC Byron C. Calhoun, MC, USAF; Laura S. Martin, M.D.; MAJ Diane M. Flynn, MC; COL Romeo P. Perez, MC; COL Roderick F. Hume, MC

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** How do you teach mentors? How do you provide the increased faculty and fellow time during downsizing? What are the optimal parameters for the mentoring process?

**Technical Approach:** Multidimensional system of educational intervention with use of MENTOR TOOL to track scholarly activity, realistic time-management tools, directive advice and goal setting for novices. Use of CREOG & ABOG scores, number of IRB approved protocols, abstracts, publications, visiting speaker, and personal satisfaction survey to measure outcome of formal mentor process. Now formal and informal focus group methodologies (survey) and review of existing GME files used to document scholarly productivity.

**Progress:** Initial tools developed, presented at MRD 2000 by COL William O. Walker. Preliminary data from existing files used to compare several year cohorts (anonymous). Survey tool from PED (WOW) to be adopted for OB-GYN use for survey.

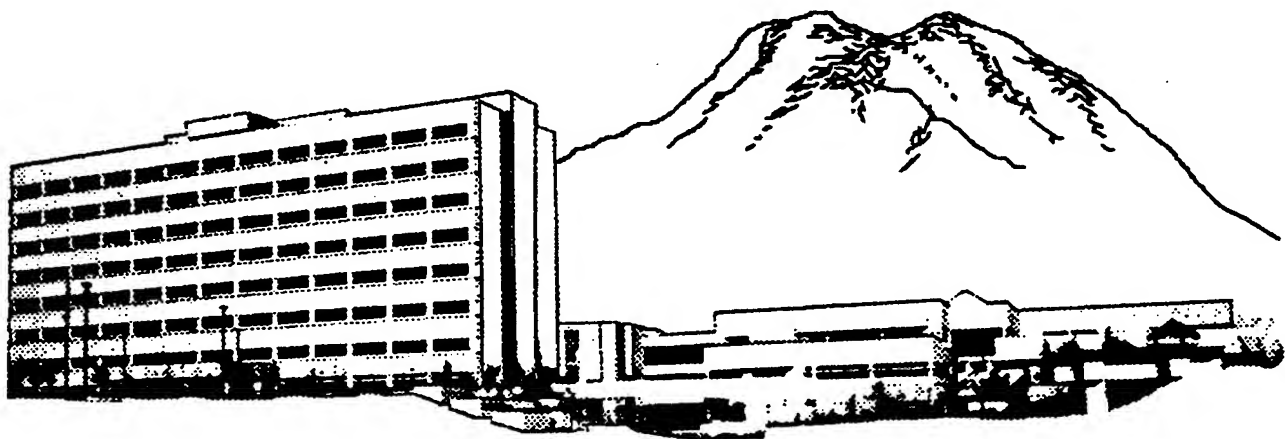
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/128	<b>Status:</b> Ongoing
<b>Title:</b> US Navy Female Service member Readiness: A Leader's Guide-Implementation Phase: Utility Validation Survey		
<b>Principal Investigator:</b> LCDR Robin E. Wood, MD, USN		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Tiffany Vara, MSC, USAR; LCDR Mary G. Battaglia, NC, USNR; LTC Byron C. Calhoun, MC, USAF; COL Robert E. Ricks, MC		
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> Sep 01	<b>Periodic Review:</b> N/A

**Study Objective:** Development of the FSRG for the AD US Army and US AF female service member has been successful. WRMC also serves USN. Cultural literate translation of FSRG for USN complete, and now survey for formal and informal focus group feedback needed to validate tool.

**Technical Approach:** Publication and distribution of GUIDE to line (fleet) unit leadership for formal and informal focus group feedback.

**Progress:** USN Guide Development completed and presented for approval by USN OG OTSG Consultant. Impact with BNH Obstetrical Naval personnel to field trial just as was done on Ft. Lewis for Female Soldier Readiness Guide.



## Detail Summary Sheets

Maternal-Fetal Medicine,  
Department of Obstetrics/Gynecology

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/002	<b>Status:</b> Ongoing
<b>Title:</b> Early Test for Preeclampsia Using Fetal Cells in Maternal Blood		
<b>Principal Investigator:</b> LTC Byron C. Calhoun, MC, USAF		
<b>Department:</b> OB/GYN, MFM		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Roderick F. Hume, MC; MAJ Elizabeth G. Hancock, MC; MAJ Christina Apodaca, MC; MAJ Brian T. Pierce, MC; ; ;		
<b>Start Date:</b> 10/26/1999	<b>Est. Completion Date:</b> Jul 00	<b>Periodic Review:</b> N/A

**Study Objective:** To test whether there are increased numbers of fetal erythroblasts in patients at risk for severe preeclampsia.

**Technical Approach:** This protocol seeks to enroll 150 singleton, uncomplicated nulligravida patients at 16-20 weeks in a prospective cohort study. Patients will be selected on the basis of uterine artery Doppler flow abnormalities. A cohort of normal, uncomplicated, nulligravida patients with normal uterine artery Dopplers will serve as controls. Presently anatomy surveys are performed on virtually all pregnant women at 16-20 weeks at this time and the examinations will add only 10-15 minutes per exam. All patients will have 20 ccs of maternal blood drawn at 16-20 week ultrasound and 4-6 weeks later and sent to our co-investigators (at their expense) for analysis of fetal erythroblasts. The co-investigators will be blinded to the uterine artery Doppler studies and demographics until after completion of the study when correlation between uterine Doppler studies, fetal erythroblasts, and preeclampsia will be done. For analysis will be done using Mann-Whitney test for non parametric data (SPSS Statistic package).

**Progress:** No work was done on this protocol during FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/094      **Status:** Ongoing

**Title:** Hispanic Ethnicity and the Relationship of Ultrasound Criteria for Attributable Risk for Aneuploidy

**Principal Investigator:** LTC Byron C. Calhoun, MC, USAF

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** CPT Jannifer A. Brown, MC; MAJ Elizabeth G. Hancock, MC; CPT Lisa M. Foglia, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** To determine ultrasound growth curves from the database presently in place from the MAMC IRB approved protocol #96164 (Natural History of Gallbladder Disease in Pregnancy) and develop ethnic specific growth curves with attributable risk for aneuploidy based ultrasound derived criteria.

**Technical Approach:** This retrospective study of previously existing files will look at fetal measurements at varying times during gestation. Measurements obtained on Hispanic patients will be compared to those of Asian, Caucasian, and Black patients to determine what is considered normal growth for Hispanic patients. Predictions of aneuploidy will be evaluated against birth records as well as prenatal chromosomal analysis by amniocentesis when available. This information will allow comment on the accuracy and applicability of femur length as a minor ultrasound risk adjustment for aneuploidy specific to a Hispanic population.

**Progress:** 983 records have been reviewed in FY00. Record review will continue as they become available.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/131

**Status:** Ongoing

**Title:** Comparative Study of US Detected Fetal Anomalies and Maternal Age in Two Healthcare Systems (Referral versus Routine Screening)

**Principal Investigator:** LTC Byron C. Calhoun, MC, USAF

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** Laura S. Martin, M.D.; Mark I. Evans, Professor; COL Roderick F. Hume, MC

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** What if any effect does maternal age play in prenatal detection of fetal anomalies? Is there a difference between two healthcare delivery systems in the detection rates for fetal anomalies according to maternal age or type of anomaly (minor, major, multiple)?

**Technical Approach:** Epidemiologic comparative analyses of existing data of US findings stratified by maternal age and type of fetal anomaly, fetal or neonatal karyotype, and neonatal confirmation of findings when available (+MAMC, -wsu).

**Progress:** This protocol recently received review and approval by the IRB. No work was initiated on this study in FY00.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 98/068	Status: Ongoing
Title: The Expression of Adrenomedullin and Its Receptor in the Human Placenta		
Principal Investigator: LTC Byron C. Calhoun, MC, USAF		
Department: OB/GYN, MFM	Facility: MAMC	
Associate Investigator(s): MAJ Richard K. Wagner, MC; Katherine H. Moore, Ph.D.; MAJ Christina Apodaca, MC; COL Roderick F. Hume, MC		
Start Date: 5/22/1998	Est. Completion Date: Sep 98	Periodic Review: 3/28/2000

**Study Objective:** To elucidate the expression of adrenomedullin (ADM) and its receptors in specific tissue components of the human placenta. This will be investigated by using placental tissue from both uncomplicated pregnancies and pregnancies complicated by chronic hypertension and pregnancy induced hypertension. Western blot analysis will be used to identify adrenomedullin expression. Reverse transcriptase-polymerase chain reaction will be used to identify the expression of adrenomedullin messenger ribonucleic acid for ADM and to identify presence of the ADM receptor. Immunocytochemical analysis will also be used to establish the expression of ADM in specific placental tissues.

**Technical Approach:** Adrenomedullin is a potent vasoactive peptide, whose vasoactive properties have been extensively described. It has been isolated from various human tissues, including pheochromocytoma, lung, heart and pancreas. Its presence in human plasma suggests that it functions as a circulating hormone, influencing the perfusion of various organs. The presence of adrenomedullin has recently been described in fetal membranes and amniotic fluid, suggesting its role in fetal perfusion. Increases of adrenomedullin in pathologic states have been described, including renal failure and hypertension in non-pregnant individuals, and in pregnant women with preeclampsia. To date there exist no studies demonstrating the isolation of adrenomedullin and its receptor in specific placental tissues. We will isolate samples of amnion, cotyledon, umbilical artery and umbilical vein from women with uncomplicated pregnancies and pregnancies complicated by pregnancy induced hypertension. Western blot analysis will be used to identify the presence of the adrenomedullin protein. Reverse transcriptase-polymerase chain reaction will be used to isolate total messenger ribonucleic acid for adrenomedullin and its receptor. Histochemical staining will be used to identify adrenomedullin in the tissue samples. Categorical analysis will be performed describing the distribution of adrenomedullin and its receptor in both normal placentas and the placentas from patients with chronic hypertension and pregnancy induced hypertension.

**Progress:** 8 placentas were examined in FY00, (5 from normal pregnancies, 3 from pregnancies complicated by oligohydramnios). Adrenomedullin and adrenomedullin receptor mRNAs were identified in all tissue components of the placentas tested. Within the normal placentas, the expression of adrenomedullin mRNA and adrenomedullin receptor mRNA did not differ statistically between the tissue components. Within the placentas from patients with oligohydramnios, the expression of adrenomedullin and adrenomedullin receptor mRNA did not differ statistically between the tissue components. However, when comparing normal to oligohydramnios placentas, there was a five-fold increase in adrenomedullin mRNA and a three-fold increase of adrenomedullin receptor mRNA in placentas from patients with oligohydramnios. Adrenomedullin immunoreactivity was present in all tissues studied. The increased adrenomedullin mRNA in the umbilical artery and elevated adrenomedullin receptor mRNA in the cotyledons of placentas from patients with oligohydramnios may represent a local fetoplacental physiologic adaptive response to vascular compromise. This study remains ongoing at Madigan Army Medical Center.



### Detail Summary Sheet

Date: 29 Sep 00

Number: 99/075

Status: Completed

Title: Fetal Macrosomia in a Military Population

Principal Investigator: LTC Byron C. Calhoun, MC, USAF

Department: OB/GYN, MFM

Facility: MAMC

Associate Investigator(s): CPT Curt A. Misko, MC; MAJ Elisabeth Hancock, MC; CPT Lisa M. Foglia, MC

Start Date:  
6/22/1999

Est. Completion Date:  
Sep 99

Periodic Review:  
5/23/2000

**Study Objective:** To determine the incidence of macrosomia (> 4500 gm) in the military population and evaluate for co-morbidities.

**Technical Approach:** This study will try to determine that macrosomic fetuses are increased in incidence in the military population with variables of interest to include, fetal and maternal morbidities associated with macrosomic fetuses. The inherent risks associated with fetal macrosomia at delivery that will be evaluated are: shoulder dystocia, fetal hypoglycemia, hypercalcemia, hyperbilirubinemia, trauma to maternal birth canal, maternal hemorrhage and increased risk of cesarean section. This will be done by chart review for 200 patients to be compiled with 100 patients from a similar study by Keesler AFB for publication and presentation. We will review charts starting at the end of 1998 and going back until 100 macrosomic infants are found. At the same time 100 patients will be used as controls by choosing the nearest non-macrosomic patient (birth weight <4000gms) to the macrosomic patient.

**Progress:** This study was reported as completed, 9 May 00. Maternal and fetal demographics were obtained on 113 consecutive macrosomic infants (>4500 gm) delivered between 1 Jan 95 and 30 Jun 98 at Keesler and Madigan Army Medical Centers. Control infants were obtained by matching the next infant in the delivery log weighing <3500 gm with similar maternal age (+ 2 yr) and estimated gestational age (+ 1 wk). Clinical variables between the two groups were compared using logistic regression and Chi square tests

**Results:** Body mass index, Leopold estimated fetal weight (>8 lbs) and intrapartum fundal height >38 cm were associated with an increased risk of fetal macrosomia ( $p=0.01$ ,  $0.03$  and  $0.0009$  respectively). Total pregnancy weight gain, third trimester weight gain, and 1-hr glucola test were not associated with delivering a macrosomic infant ( $P=.45$ ,  $.08$ , and  $.24$ , respectively). Fundal heights >38 cm was associated with a 20 times greater risk of delivering a macrosomic infant while Leopold's estimated weight >8 lbs is associated with a 6-fold increase risk. Conclusion: While no maternal variable is a consistent predictor of delivering a macrosomic infant, maternal body mass index, Leopold's estimated fetal weight, and intrapartum fundal height appear to be the best predictors of delivering a large infant.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/100

**Status:** Ongoing

**Title:** Comparison of First and Second Trimester Screening for Prenatal Detection of Down Syndrome and Other Birth Defects ( FASTER )

**Principal Investigator:** LTC Byron C. Calhoun, MC, USAF

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** MAJ Christina Apodaca, MC; MAJ Brian T. Pierce, MC; LTC Peter E. Nielsen, MC; Laura S. Martin, M.D.; COL Roderick F. Hume, MC; V Souter

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
Jul 01

**Periodic Review:**  
9/26/2000

**Study Objective:** (1) To determine the effectiveness of first trimester screening in detection of fetal chromosome abnormalities as well as other birth defects and to compare the accuracy of first trimester screening with second trimester screening, and (2) to evaluate patient assessment of perceived risk compared to calculated risk of fetal Down syndrome and other birth defects.

**Technical Approach:** Patients will be enrolled between 10.5 and 14 weeks. They will be asked to complete a questionnaire to evaluate their perceived risk of fetal Down's syndrome and their attitudes toward patient screening. First trimester ultrasound with maternal-blood sampling in will be performed 10 3/7 weeks and 13 6/7 weeks looking for nuchal (neck thickness) with a follow-up ultrasound in the second trimester between 15 and 20 weeks.

First trimester laboratory testing will include maternal-serum for free Beta-human chorionic gonadotropin and pregnancy associated plasma protein-A (PAPP-A). The second trimester testing will include alpha-fetoprotein (AFP), unconjugated estriol (uE3), and human chorionic gonadotropin (hCG) as well as inhibin-A. Further, the patients who screen positive in either first or second trimester analyte screening will have maternal blood sent to be included in the "National Institute of Child Health and Human Development Fetal Cell Isolation Study (NIFTY). This study seeks to explore the ability to extract fetal cells from maternal blood for possible detection of abnormal chromosomes.

**Progress:** No work was done on this protocol in FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/091

**Status:** Ongoing

**Title:** Magnesium in Preeclampsia: Plasma (maternal & fetal) and Placental Levels of Ionized Magnesium

**Principal Investigator:** MAJ Elisabeth Hancock, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** COL Roderick F. Hume, MC; LTC Byron C. Calhoun, MC, USAF; CPT Todd M. Rossignol, MS; ;

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
N/A

**Study Objective:** To determine maternal blood levels of ionized magnesium (IMg) before and after delivery, fetal (umbilical) blood levels of IMg at delivery and placental IMg levels at delivery.

**Technical Approach:** Maternal venous blood, placental samples, and umbilical blood will be collected from the following subjects during labor and delivery: 25 preeclamptic patients, 25 patients in preterm labor, and 25 patients in uncomplicated term labor. Sodium, potassium, ionized calcium, and ionized magnesium will be measured. Results will be analyzed to determine if there is a significant deviation in levels of blood chemicals for different pregnancy conditions.

**Progress:** 12 samples have been collected. The protocol remains ongoing at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/108	<b>Status:</b> Completed
<b>Title:</b> Maternal Lipid Metabolism and Pregnancy Outcome		
<b>Principal Investigator:</b> MAJ Elisabeth Hancock, MC		
<b>Department:</b> OB/GYN, MFM	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Byron C. Calhoun, MC, USAF; MAJ Brian T. Pierce, MC; CPT Jude Abadie, MS; LTC Jerome B. Myers, MC; Troy H. Patience, B.S.; Laura S. Martin, M.D.; COL Roderick F. Hume, MC		
<b>Start Date:</b> 7/25/2000	<b>Est. Completion Date:</b> Jul 01	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to establish normal values for total cholesterol, LDL, HDL, Triglyceride, lipoprotein (a), apolipoproteins and fasting glucose at various gestational ages in human pregnancy. Establishment of normal values will provide a standard along with patient demographic information to which outliers can be compared. Future studies will be directed at identifying lipid levels that are associated with adverse or beneficial effect on pregnancy outcome.

**Technical Approach:** Normal human pregnancy result is a pronounced physiologic hyperlipidemia involving a gestational rise in blood triglycerides by 300% and cholesterol by 50% at term. Pregnancy exerts an adverse effect on the total/DL cholesterol ratio that has been implicated in the increased incidence of cardiovascular disease in women of high parity. Women with preeclampsia display additional alterations in blood lipids reflecting a disordered lipid metabolism. This study will examine charts to determine a standard lipid profile for preeclampsia versus matched controls. These established profiles may lead to development of multiple logistic analysis tools as screening tests for various adverse pregnancy outcomes.

**Progress:** 1816 charts were reviewed during FY 2000. Results: data confirms that the "supraphysiologic" normal values for serum total cholesterol (239 +/- 43mg/dl) and total triglycerides (210 +/- 75) at 28-32 weeks established by previous small studies in homogenous populations can be extrapolated to the general population. Patients with a triglyceride level 2 standard deviations above the mean had a significantly greater rate of preeclampsia compared to the remainder of the population. Conclusion: Serum lipid profiles may be useful in predicting an individual pregnant woman's risk of developing preeclampsia.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/051

**Status:** Ongoing

**Title:** The Use of Transvaginal Sonography in Predicting Preterm Delivery in Patients with Preterm Contractions

**Principal Investigator:** CPT Christine M. Kovac, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** CPT Lisa M. Foglia, MC; MAJ Brian T. Pierce, MC; MAJ Richard K. Wagner, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF; Troy H. Patience, B.S.; MAJ Christina Apodaca, MC

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Aug 99

**Periodic Review:**  
3/28/2000

**Study Objective:** Primary: To investigate the accuracy of transvaginal cervical ultrasound in predicting the occurrence of preterm delivery, in patients presenting to Labor and Delivery with complaints consistent with preteen contractions

Secondary: We will also compare the abilities of transvaginal sonography and digital cervical exam in predicting preterm delivery within one week from examination.

**Technical Approach:** Despite recent advances in modern obstetric care, the incidence of preterm delivery has not decreased, and remains a leading cause of neonatal morbidity and mortality. Due to the refractory nature of preterm labor to effective management, early diagnosis is essential. Definitive diagnosis of legitimate preterm labor remains difficult, however, and results in over-diagnosis and treatment of what is most likely innocuous preterm contractions.

Early cervical effacement and dilation may be subtle changes that may not be identified on digital examination. Transvaginal cervical ultrasonography is a precise, reproducible, modality that can provide an objective means by which to evaluate the cervix for early effacement and dilation.

While studies have identified the utility of transvaginal cervical sonography in predicting preterm delivery, its role in assessing patients with preterm contractions is less clear.

We propose to evaluate the utility of transvaginal cervical sonography in predicting subsequent preterm labor and delivery. We will also compare the efficacy of cervical sonography with digital examination in predicting the incidence of preterm delivery.

We hope to identify a cervix length in a patient with preterm contractions, at which a physician can feel comfortable sending her home, with a 98 to 100 percent assurance that she will not deliver within the next week (eg, that cervical length which yields a 98 to 100 percent negative predictive value for preterm delivery within a week).

**Progress:** Two patients have been enrolled in this study in FY00 at MAMC. A change of principal investigator was approved due to the PCS of Dr. Apodaca to TAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/035

**Status:** Ongoing

**Title:** Comparison of Elective Labor Induction and Spontaneous Labor: A Randomized, Controlled Clinical Trial

**Principal Investigator:** CPT Penny L. Larson, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** CPT Robert H. G. Holland, MC; COL Paul N. Smith, MC; MAJ Brian T. Pierce, MC; MAJ Richard K. Wagner, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF; COL Romeo P. Perez, MC; Kathleen Judge; Roxanne Piecek; CPT Miguel A. Brizuela, MC; MAJ Christina Apodaca, MC

**Start Date:**  
2/23/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
3/28/2000

**Study Objective:** The purpose of this study is to compare cesarean section rates between patients delivered at term with a favorable cervix by elective induction with patients allowed to enter labor spontaneously. Additional maternal and neonatal outcomes will also be compared between the two groups.

**Technical Approach:** Between 38 and 39 weeks, subjects presenting with a favorable cervix and consenting to be in the study, will be randomized into either the labor induction group or the spontaneous labor group. Labor induction will follow MAMC Labor and Delivery protocol. Those subjects assigned to labor induction will be scheduled within 72 hours for admission including routine admission labs, establishment of intravenous access and fetal monitoring. Subjects in the control group will continue in the Obstetric Clinic until the onset of spontaneous labor. Their labor will also follow MAMC Labor and Delivery protocol.

Subject information sheets for the health care providers managing the subjects will capture complete documentation of labor and delivery information. These data will be entered into a computer database for analysis and the data sheets will not be part of the subject's medical record. Subjects will also be asked to fill out a questionnaire, the Labor and Delivery Satisfaction Index, to assess satisfaction with their labor and delivery

Chi-square analysis will be used to assess for differences in nominal variables (epidural use, oxytocin use, chorioamnionitis, postpartum complications, NICU admissions, meconium stained amniotic fluid, neonatal or maternal complications, neonatal or maternal birth trauma). The paired Student's t-test will be used to compare groups of continuous variables (cesarean section rate, vaginal delivery rate, operative vaginal delivery rate, duration of first and second stage of labor, maternal and neonatal lengths of stay, birth weight, Apgar scores).

**Progress:** This study enrolled 16 subjects in FY99 and 14 subjects in FY00 for a total enrollment of 30. There was a change of principal investigator due to the PCS of Dr. Apodaca to TAMC, Jul 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/055	<b>Status:</b> Ongoing
<b>Title:</b> Fetal Growth Curves in a Military Population		
<b>Principal Investigator:</b> MAJ Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN, MFM	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Brian T. Pierce, MC; MAJ Richard K. Wagner, MC; MAJ Elisabeth Hancock, MC; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC; LTC Byron C. Calhoun, MC, USAF; MAJ Christina Apodaca, MC		
<b>Start Date:</b> 3/28/2000	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the range of in utero fetal weight throughout pregnancy using actual data, including birth weights, for a cohort at sea level using a database presently in place from the MAMC IRB approved protocol #96164 (natural history of gallbladder disease in pregnancy) and develop specific growth curves relevant to our population.

**Technical Approach:** Retrospective review of previously existing files and medical records. Data collected will include sonographic measurements of active duty women and military health care beneficiaries, plus maternal age, ethnic origin, smoking status, monthly income, neonatal gender and neonatal birth weight.

**Progress:** Ultrasound measurements were reviewed of over 1200 women longitudinally throughout their pregnancies. This data was used to compare with 6 different major ultrasound growth curves. Results: The Hadlock growth curve most closely matched that of our racially mixed, culturally diverse military community. Data collection continues on term ultrasound biometry to add to the current data set which was unavailable at the time of the earlier reported results. Dr. Napolitano assumed the role of PI, July 00, due to PCS of Dr. Apodaca to TAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/013

**Status:** Ongoing

**Title:** The Effects of Hypoxia and Hypoxia with Acidemia on Placental Production of Interleukin-6 in the Isolated Dually Perfused Placental Cotyledon

**Principal Investigator:** MAJ Brian T. Pierce, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** MAJ Peter G. Napolitano, MC; MAJ Christina Apodaca, MC; MAJ Elizabeth G. Hancock, MC; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
N/A

**Study Objective:** To determine the effects of hypoxia and hypoxia with acidemia on placental production of interleukin-6 (IL-6).

**Technical Approach:** This protocol will isolate and study 2 cotyledons from the placentas of 10 uncomplicated term pregnant patients. One cotyledon will have the maternal and fetal circuit perfused with a hypoxic and non-acidemic Hanks Balanced Solution at physiologic rate (4 cc/min). The other cotyledon will have the maternal and fetal circuit perfused with both a normoxic and non-acidemic Hanks Balanced Solution, also at physiologic rate. Effluents for IL-6 determination will be collected from the fetal circulations at hourly intervals. Perfusion will be maintained for four hours. Vascular tone in the fetal compartment will be continuously monitored throughout the experiment and recorded at 10-min intervals. These results will be compared to existing data from prior perfusion studies.

The second part of this study will also study 2 cotyledons each from 10 uncomplicated term pregnancies. One cotyledon perfused with a hypoxic and acidemic Hanks Balanced Solution at physiologic rate (4 cc/min). The other cotyledon will have the maternal and fetal circuit perfused with both a normoxic and non-acidemic Hanks Balanced Solution, also at physiologic rate. Again, effluents for IL-6 determination will be collected from the fetal circulations at hourly intervals. Perfusion will be maintained for four hours. Vascular tone in the fetal compartment will be continuously monitored throughout the experiment and recorded at 10-min intervals.

These results will be compared to existing data (both IL-6 concentrations and pressure recordings) from prior perfusion studies involving physiologic conditions and different perfusion rates.

**Progress:** Five placentas were divided into two cotyledons each. One cotyledon was perfused under hypoxic conditions, while the other cotyledon was perfused under hyperoxic conditions. Fetal effluents were collected every hour for four hours and fetal vascular tone was recorded every ten minutes. IL-6 concentrations were determined by ELISA. Results: Hyperoxic conditions had a statistically significant increase in IL-6 production, while the hypoxic condition resulted in lower perfusion pressures.



### Detail Summary Sheet

Date: 29 Sep 00

Number: 200/015

Status: Ongoing

**Title:** Myometrial Gap Junctions and Their Importance in Obstetric Patients with Chorioamnionitis

**Principal Investigator:** MAJ Brian T. Pierce, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** Lisa M. Pierce, D.Sc.; Alan F. Lau, Ph.D.; MAJ Christina Apodaca, MC; MAJ Richard K. Wagner, MC; LTC Peter E. Nielsen, MC; COL Roderick F. Hume, MC

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
N/A

**Study Objective:** The purpose of this study is to investigate whether decreased connexin 43 mRNA and/or protein levels and the decreased formation of gap junction plaques in the myometrium is responsible, at least in part, for the lack of high amplitude, well-coordinated contractions occurring during labor and postpartum in patients with chorioamnionitis.

**Technical Approach:** Myometrial tissue will be obtained during cesarean section from laboring patients with and without chorioamnionitis, and from those patients requiring cesarean section prior to the onset of labor (without chorioamnionitis). Cx43 messenger RNA and protein levels will be compared among these patients and immunohistochemistry will be performed to examine the presence of gap junction plaques. Decreased Cx43 mRNA and protein levels and decreased gap junction formation in the myometrium of chorioamnionitis patients may lead to decreased gap junctional communication (GJC) in the myometrium. This decreased GJC may be responsible, at least in part, for the lack of high amplitude, well-coordinated contractions occurring during labor and postpartum in patients with chorioamnionitis.

**Progress:** 35 uterine biopsies were taken from patients undergoing caesarian section. Connexin 43 (Cx43) mRNA and protein were determined by Northern and Western analysis, respectively. Data was analyzed according to labor characteristics. Results: Expression of Cx43 mRNA increased during labor ( $p < 0.05$ ). There was a trend for Cx43 protein to decrease during normal labor when compared to patients not in labor or with dysfunctional labor ( $p = 0.09$  and  $p = 0.07$ , respectively). Cx43 protein expression was positively correlated to the strength of uterine contractions for all laboring patients and negatively correlated to cervical dilation for patients with dysfunctional labor and chorioamnionitis ( $p < 0.05$ ). Conclusion: High amplitude uterine contractions, the hallmark of normal labor, are associated with increased Cx43 protein expression. Aberrant Cx43 protein expression appears to play a role in dysfunctional labor, specifically when complicated by chorioamnionitis.

### Detail Summary Sheet

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<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/024	<b>Status:</b> Ongoing
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**Title:** The Effects of Shear Stress on Placental Production of Vascular Endothelial Growth Factor (VEGF), Placental Growth Factor (PLGF), and Tumor Necrosis Factor (TNF-alpha) in the Isolated Dually Perfused Placental Cotyledon

**Principal Investigator:** MAJ Brian T. Pierce, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** Lisa M. Pierce, D.Sc.; MAJ Christina Apodaca, MC; MAJ Peter G. Napolitano, MC; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF

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**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Dec 00

**Periodic Review:**  
N/A

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**Study Objective:** To determine the effects of shear stress on placental production of vascular endothelial growth factor (VEGF), placenta growth factor (PIGF), and tumor necrosis factor-a (TNF-a).

**Technical Approach:** Placental effluents from a prior study are available for evaluation of placental response of these molecules. The effluents were collected in the following manner:

Paired cotyledons from 5 placentas obtained from uncomplicated vaginal and cesarean deliveries in MAMC's labor and delivery were used. A perfusate consisting of Hank's balanced salt solution, bovine albumin, heparin, and gentamicin was used to perfuse both the maternal and fetal circulations of the cotyledons. One cotyledon had the fetal circulation infused at 1 cc/min. The other cotyledon had the fetal circulation perfused at 10 cc/min. After establishing perfusion of an intact fetoplacental circuit, effluents were collected at hourly intervals for four hours. These samples were stored for determination of IL-6 levels by ELISA. The fetoplacental vascular tone was continuously monitored throughout the experiment and recorded at 10-min intervals. Data was analyzed using repeated measure analysis of variance.

**Progress:** Five placentas were divided into two cotyledons each. One cotyledon was perfused at a high perfusion rate (10 cc/min), the other at a low perfusion rate (1 cc/min). Fetal effluents were collected hourly for four hours and VEGF, P1GF, and TNF concentrations were determined by ELISA. Results: VEGF and P1GF were not detected in the fetal effluents under either condition. TNF was significantly elevated under the low perfusion rate conditions. Conclusion: VEGF and P1GF are not acutely produced by the placenta during hypoperfusion. Hypoperfusion may be related to cerebral palsy, in that elevated inflammatory cytokines are a hallmark of the fetal inflammatory response syndrome, and placental pathology is a common finding in fetuses who subsequently develop CP.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/029

**Status:** Ongoing

**Title:** The Effects of Hypoxia and Hypoxia with Acidemia on Placental Production of Vascular Endothelial Growth Factor and Placenta Growth Factor in the Isolated Dually Perfused Placental Cotyledon

**Principal Investigator:** MAJ Brian T. Pierce, MC

**Department:** OB/GYN, MFM

**Facility:** MAMC

**Associate Investigator(s):** Lisa M. Pierce, D.Sc.; MAJ Peter G. Napolitano, MC; MAJ Christina Apodaca, MC; MAJ Elizabeth G. Hancock, MC; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Dec 00

**Periodic Review:**  
N/A

**Study Objective:** To determine the effects of hypoxia and hypoxia with acidemia on placental production of vascular endothelial growth factor (VEGF), placenta growth factor (PlGF), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ).

**Technical Approach:** Paired cotyledons from 20 placentas will be obtained from uncomplicated vaginal and cesarean deliveries in MAMC's labor and delivery. A perfusate consisting of Hank's Balanced Salt Solution, bovine albumin, heparin, and gentamicin will be used to perfuse both the maternal and fetal circulations of the cotyledons. The first 10 placentas will be divided into 2 cotyledons, one perfused with a hypoxic solution, the other (control) perfused with a physiologic solution. The next 10 placentas will also be divided into 2 cotyledons, one perfused with a hypoxic and academic solution, the other (control) perfused with a physiologic solution. After establishing perfusion of an intact fetoplacental circuit, effluents will be collected at hourly intervals for four hours. These samples will be stored for determination of VEGF, PlGF, and TNF- $\alpha$  protein levels by ELISA. The fetoplacental vascular tone will be continuously monitored throughout the experiment and recorded at 10 minute intervals. Data will be analyzed using repeated measure analysis of variance.

**Progress:** Five placentas were divided into two cotyledons each. One cotyledon was perfused under hypoxic conditions and the other was perfused under hyperoxic conditions. Fetal effluents were collected hourly for four hours and VEGF and PlGF were determined under ELISA. Results: VEGF and PlGF were not detected in the fetal effluents under either condition. Conclusion: VEGF and PlGF are not acutely produced by the placenta during fetal hypoxia.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/096	<b>Status:</b> Ongoing
<b>Title:</b> The Effects of Hypoxia and Hypoxia With Acidemia on Placental Production of Adrenomedullin in the Isolated Dually Perfused Placental Cotyledon		
<b>Principal Investigator:</b> MAJ Brian T. Pierce, MC		
<b>Department:</b> OB/GYN, MFM	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Christina Apodaca, MC; MAJ Peter G. Napolitano, MC; Lisa M. Pierce, D.Sc.; COL Roderick F. Hume, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF		
<b>Start Date:</b> 6/27/2000	<b>Est. Completion Date:</b> Oct 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if adrenomedullin levels are increased in placental cotyledons exposed to hypoxic and academic conditions.

**Technical Approach:** Cotyledons from a total of 20 placentas will be obtained from patients with uncomplicated term vaginal and caesarian deliveries. Maternal and fetal circulations of the cotyledons will be perfused with a solution of Hank's Balanced Salt Solution, bovine albumin, heparin and gentamicin. The 2 cotyledons from the first 10 placentas will be perfused, one with hypoxic solution and the other (control) with physiologic solution. Two cotyledons each from the next 10 placentas will be perfused, one with hypoxic and academic solution and the other (control) with physiologic solution. After perfusion of an intact fetoplacental circuit has been established, effluents will be collected at hourly intervals for four hours. These samples will be batched and stored for adrenomedullin quantitation, using an ELISA. Fetoplacental vascular tone will be continuously monitored throughout the experiment and will be recorded at ten-minute intervals. Data will be analyzed using repeated measure analysis of variance.

**Progress:** Five placentas were divided into two cotyledons each. One cotyledon was perfused under hypoxic conditions, while the other cotyledon was perfused under hyperoxic conditions. Fetal effluents were collected hourly for four hours and frozen at -70 degrees Celsius for future determination of adrenomedullin concentration.

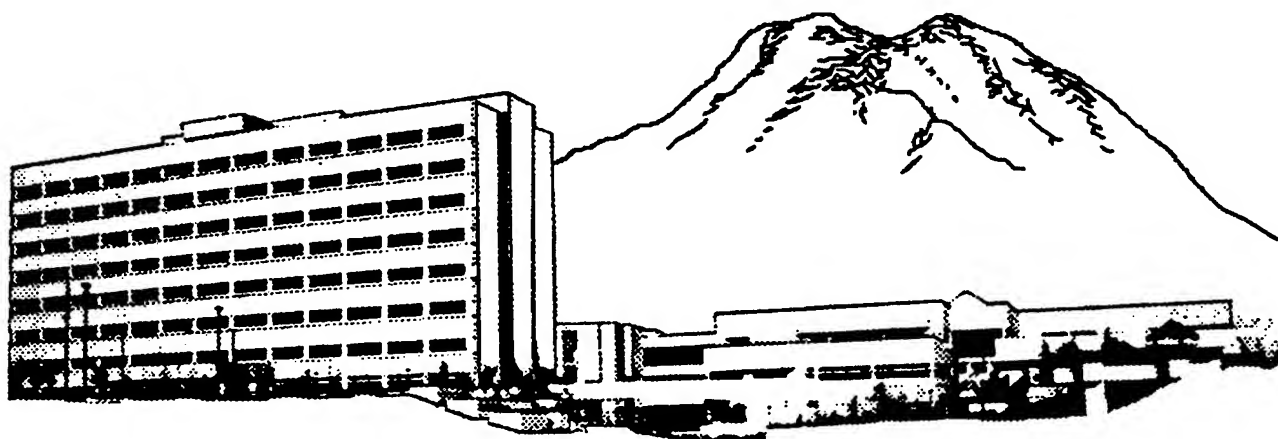
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/026	<b>Status:</b> Completed
<b>Title:</b> The Relationship Among Fetal Karyotype, Intrauterine Fetal Death, and Histologic Villous Mineralization		
<b>Principal Investigator:</b> MAJ Brian T. Pierce, MC		
<b>Department:</b> OB/GYN, MFM		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Roderick F. Hume, MC; Laura S. Martin, M.D.; MAJ Sandra Carter, MC; LTC Peter E. Nielsen, MC; LTC Byron C. Calhoun, MC, USAF; CM Salafia		
<b>Start Date:</b> 1/26/1999	<b>Est. Completion Date:</b> Dec 99	<b>Periodic Review:</b> N/A

**Study Objective:** To describe the relationship between fetal death and degree of villous mineralization of the placenta in aneuploid fetuses.

**Technical Approach:** Records of all chromosomal analysis obtained on fetuses and newborns at Madigan AMC will be reviewed (from Jan 1992 through Jul 1998). Available placentas will be sampled according to standard protocol and reviewed by a pathologist for evidence of villous mineralization. The reviewing pathologist will be blinded to both the karyotype of the placenta and the clinical history (liveborn or stillborn).

**Progress:** Records of all chromosomal analyses obtained on fetuses and newborns at MAMC were reviewed from Jan 1992 to Jul 1998. Clinical histories were obtained through retrospective chart review. Available placentas were sampled according to a standard protocol. Slides were reviewed blinded to clinical or karyotypic data. Villous mineralization (VM) were considered to be absent if no VM were observed in 10 10x fields of view. VM were graded as scant if any Villi with VM seen in fewer than 5 of 40 10x fields reviewed per case. VM were considered to be many if seen in any villi in 5-20 of the 10 total fields review. VM were considered dense if seen more frequently. Results: Forty-three abnormal karyotypes were recorded, with 14 available surgical specimens. Comparing absent or scant VM to many/dense VM, stillbirth was significantly more frequent, (Chi-squared = 1.67,  $P < 0.01$ ). Conclusions: VM are more frequent in stillbirth, but may not develop post-mortem. VM are seen in liveborn infants, and may be more prevalent with severe fetal cardiac pathology. In stillborn infants, the most extensive VM are seen in Monosomy X with cystic hygroma. This study suggests that VM may indicate a mechanism of death in a stillbirth or method of chronic intrauterine compromise in a living fetus, focusing on fetoplacental circulatory compromise.



## Detail Summary Sheets

Urogynecology,  
Department of Obstetrics/Gynecology

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/108	<b>Status:</b> Completed
<b>Title:</b> A Pilot Study for Transanal Ultrasonography (TAUS) in the Repair of Episiotomy Anal Sphincteroplasty		
<b>Principal Investigator:</b> COL Gary D. Davis, MC		
<b>Department:</b> OB/GYN, UG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Jerome L. Buller, MC; COL Milo L. Hibbert, MC; COL Lawrence A. Decker, MC; LTC George McClure, MC; LTC Frederick B. Brown, MC; COL Romeo P. Perez, MC; LTC (Ret) Richard A. Sherman, MS; MAJ Patrick J. Woodman, MC		
<b>Start Date:</b> 6/20/1997	<b>Est. Completion Date:</b> Nov 97	<b>Periodic Review:</b> 7/27/2000

**Study Objective:** To assess the efficiency of intra-operative transanal ultrasound (TAUS) in the repair of the anal sphincter at episiotomy.

**Technical Approach:** Transanal ultrasonography (TAUS) has proven to be an effective means of assessing the structure and function of both the internal and external anal sphincters. Preliminary studies at Madigan Army Medical Center have shown that the intra-operative use of TAUS provides rapid and precise identification of both the internal and external anal sphincters, as well as immediate assessment of sphincter continuity and the success of sphincteroplasty. We propose to determine if the intra-operative use of TAUS will improve the anatomical and functional outcome of (a) episiotomy repair and (b) sphincteroplasty. (a) One hundred obstetric subjects at 28 weeks gestation or greater will be evaluated by endoanal ultrasound, pudendal nerve velocity and anal manometry to obtain initial. Episiotomies will be rendered only if obstetrically indicated. Those subjects requiring episiotomies at delivery will be randomly assigned to one of two groups. Those who will receive TAUS, and those who will not receive TAUS for episiotomy repair if episiotomy is indicated at delivery. Those subjects not requiring episiotomy will be dropped from the study. (b) In addition, twenty gynecologic subjects scheduled to undergo and sphincteroplasty will receive identical pre-operative evaluations of anal manometry, pudendal nerve velocities and endoanal ultrasonography to establish pre-operative values. They will be randomly assigned to one of two groups, those having repair with the aid of TAUS, and those undergoing sphincteroplasty without the aid of TAUS. All subjects (both obstetric and gynecologic) will be evaluated six weeks after surgery with repeat and manometry, pudendal nerve velocity and endoanal ultrasound. Pudendal nerve velocities, internal and external and sphincter length and width, manometric pressures, and pelvic organ prolapse quantification (POPQ) scores will be compared.

**Progress:** A total of 68 subjects were enrolled. The use of transanal sonography for the performance of episiotomy repair and sphincteroplasty adds significant intro-operative information and leads to an improved anatomical and functional surgical outcome when these procedures are performed by residents and fellows.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 200/058                      **Status:** Ongoing

**Title:** The Effect of Prenatal Pelvic Floor Exercises on Postpartum Pelvic Floor Function: A Two Phase Study

**Principal Investigator:** Amy L. O'Boyle, M.D.

**Department:** OB/GYN, UG

**Facility:** MAMC

**Associate Investigator(s):** COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; MAJ Stephen D. Seymour, MC; COL Romeo P. Perez, MC; LTC (Ret) Richard A. Sherman, MS; CPT Vanessa D. Dance, MC; CPT Lisa M. Foglia, MC; COL Robert E. Ricks, MC

**Start Date:**  
3/28/2000

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
N/A

**Study Objective:** To determine whether the performance of pelvic floor strengthening and control exercises (Kegel exercises and electromyographic biofeedback from the pelvic floor) prior to giving birth for the first time (primiparous) can (1) effect pelvic floor function (as measured by POPQ and transanal sonography) and urodynamic testing (UCMG - urocystometrogram) (2) decrease the occurrence and intensity of common pelvic floor problems occurring after delivery including pelvic organ prolapse, urinary incontinence, and fecal incontinence. Within this overall objective, to determine whether addition of home-use surface electromyographic (muscle tension) biofeedback devices to standard Kegel exercises will decrease the rate and intensity of problems.

**Technical Approach:** The first phase of this study will be a ten-subject open pilot to refine techniques. Each participant will perform the exercises for at least one month prior to delivery and at least two months afterwards. Feedback about the procedures and patient attitudes will be evaluated

The second phase will recruit a total 60 first-delivery mothers to three different arms of the study. Each participant will randomly be assigned to: no prescribed pelvic floor exercises in addition to standard counseling (normal treatment control group), instructed Kegel exercises (practiced at home for at least one month prior to delivery) in addition to standard counseling, or instructed Kegel floor exercises and use of the Persist Pelvic Floor trainer (a biofeedback device) at home in addition to standard counseling.

Data from all three groups will be compared to determine the effect of supplemented instruction on postpartum pelvic floor function.

**Progress:** This study has not yet received final approval at MAMC due to the PCS of its original PI, Dr. Dance.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/102

**Status:** Ongoing

**Title:** Comparison of Tolterodine and Oxybutinin for the Treatment of Urinary Incontinence Among Female Soldiers

**Principal Investigator:** Amy L. O'Boyle, M.D.

**Department:** OB/GYN, UG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Patrick J. Woodman, MC; COL Milo L. Hibbert, MC; CPT Vanessa D. Dance, MC; MAJ Stephen D. Seymour, MC; COL Romeo P. Perez, MC; CDR (Res) Dennis A. Kelly, Ph.D.; LTC (Ret) Richard A. Sherman, MS; COL Gary D. Davis, MC; COL Robert E. Ricks, MC

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
10/24/2000

**Study Objective:** (1) To determine the relative effectiveness of Tolterodine and Oxybutinin in the treatment of urinary urge incontinence in female soldiers during exercise, (2) to determine incidence and severity of anticholinergic side effects of Tolterodine and Oxybutinin in female soldiers, (3) to determine whether Tolterodine and Oxybutinin have significant cognitive effects on work performance tasks, and (4) to determine changes in quality of life and work performance during treatment of urinary urge incontinence with Tolterodine and Oxybutinin.

**Technical Approach:** Sixty active duty female soldiers with urge incontinence will be recruited through a letter sent to all female soldiers at Fort Lewis, Washington. Each subject will initially undergo a standard evaluation of the lower urinary tract. The urodynamic evaluation will include uroflometry, with post-void residual urine volume measurement, retrograde provocative water cystometry, resting and stressed urethral axis determination, and direct visualization testing of fluid loss with stress. Urethral pressure profilometry with urethral closure pressures will also be performed. The subjects will then be evaluated one week later with ambulatory cystometric recordings. The subjects will be fitted with the UPS 2020 ambulatory measurement system. The intravesical and intravaginal pressures will be recorded with flexible 3mm microtip inserted 6cm from the urethral meatus and above the levator plate vaginally. The subjects will be given instructions to record events on the keyboard of the UPS 2020 ambulatory urodynamic recording system as they occur, and to proceed with the work or exercise which commonly produce their urinary incontinence. All subjects will be asked to complete a standard questionnaire which will assess the number and severity of the incontinent episodes they are experiencing. In addition they will complete a standard questionnaire which will assess job satisfaction and a standard quality of life survey. Once baseline values for the number and magnitude of detrusor contractions have been obtained, the subjects will be randomly assigned to one of three groups: Group I - Twenty subjects will receive placebos (one tablet twice a day), Group II - Twenty subjects will receive Oxybutinin (5mg twice a day), Group III - Twenty subjects will receive Tolterodine (1 mg twice a day). All subjects will be re-tested after one week of therapy by both stationary and ambulatory urodynamic studies. Comparison will be made among the groups as to the reduction of the amplitude and frequency of uninhibited detrusor contractions. The subjects will repeat the standard questionnaire, which assess the number and severity of incontinent episodes as well as job satisfaction and quality of life. They will also list the number of times as well as rate the severity of which they experienced (1) dry mouth, (2) headache, (3) visual disturbances, and (4) inability to perspire during exercise. All subjects who still complain of urinary urge incontinence at the end of one week of therapy will have their medication increased as follows: Group I - Increased to two tablets twice a day, Group II - Oxybutinin increased to 5 mg three times a day, Group III - Tolterodine 2mg twice a day. All subjects will be re-tested at the end of the second week of therapy by both stationary and ambulatory urodynamics as well as with the cognitive test battery and the questionnaires. Comparisons will be made among the groups as to the reduction of the amplitude and frequency of inhibited detrusor contractions. The subjects will repeat the standard

questionnaire, which assess the number and severity of incontinent episodes as well as job satisfaction and quality of life. They will also list the number of times as well as rate the severity of which they experienced (1) dry mouth, (2) headache, (3) visual disturbances, and (4) inability to perspire during exercise.

**Progress:** No subjects have been enrolled in FY00, due to difficulty obtaining support from necessary departments/services. The IRB recently approved a change of principal investigator to LCDR Amy O'Boyle, with Dr. Davis continuing as associate investigator on this study.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/144

**Status:** Terminated

**Title:** Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig (*Sus scrofa*)

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** OB/GYN, UG

**Facility:** MAMC

**Associate Investigator(s):** COL Lawrence A. Decker, MC; COL Gary D. Davis, MC; COL Roderick F. Hume, MC; LTC Byron C. Calhoun, MC, USAF; MAJ Elizabeth G. Hancock, MC; MAJ Richard K. Wagner, MC; MAJ Martin L. Ladwig, MC; MAJ Christina Apodaca, MC; MAJ Patrick J. Woodman, MC; MAJ Stephen D. Seymour, MC; LTC Gregory E. Chow, MC; MAJ Peter G. Napolitano, MC

**Start Date:**  
9/19/1997

**Est. Completion Date:**  
Sep 00

**Periodic Review:**  
10/26/1999

**Study Objective:** To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing or stapling techniques. To familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy and vascular injury repair. To expand the operative endoscopy experience of OB/GYN Residents and Staff, prior to utilization in humans. Familiarity with these techniques will allow an increased margin of safety for patients in gynecologic surgery and better prepare the gynecologic surgeon to assist in general surgery patients when bowel or urinary tract procedures or repair are required. Increased operative endoscopy experience will minimize operating time and potential complications when utilized in the clinical setting.

**Technical Approach:** With the animal in the supine position, a midline incision will enter the abdomen and repair of lacerations and anastomosis will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reopened 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

**Progress:** This protocol was terminated, 19 Sep 00, as it had reached its triennial expiration date. Work on this study was never initiated at MAMC. A replacement protocol is being developed in support of the OB/GYN resident training program.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 200/016                      **Status:** Ongoing

**Title:** The Degree of Pelvic Relaxation in a General Population of Female Subjects

**Principal Investigator:** MAJ Patrick J. Woodman, MC

**Department:** OB/GYN, UG

**Facility:** MAMC

**Associate Investigator(s):** Steven E. Swift, M.D.; Susan Jackson, M.D.; Margie A. Kahn, M.D.; Val Y. Vogt, M.D.; Michelle M. Germain, M.D.; Amy L. O'Boyle, M.D.; Michael T. Valley, M.D.; Joseph Schaffer, M.D.; Marie Fidela R. Paraiso, M.D.; Deirdre R. Bland, M.D.; Mary Milner, Project Manager

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
N/A

**Study Objective:** To describe the degree of pelvic organ support in subjects presenting to nine geographically separate Obstetrics and Gynecology clinics requiring, as part of their visit, a routine pelvic exam to meet the requirements of annual gynecological health care and to evaluate the correlation of pelvic support to specific symptomatology associated with severe pelvic organ prolapse.

**Technical Approach:** Once subjects consent to be part of the study, during the standard pelvic exam a series of measurements to determine degree of pelvic relaxation will be performed as the subject performs a Valsalva or cough. These measurements will be recorded on a data collection sheet. Various biographical data will be collected and subjects will be asked 20 questions regarding their symptoms associated with pelvic prolapse. Data collected from this study will be used as an initial step in documenting the degree of pelvic organ support in a general population and analyze various suspected etiologic factors for the development of severe pelvic organ prolapse.

**Progress:** Data from 61 patients has been collected. Data analysis has not yet begun in this ongoing protocol. Recruitment goals for MAMC are for 200/250 patients. Patient enrollment continues.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 99/103

Status: Suspended

Title: Prevalence of Anal Incontinence in New Mothers Trial (PAINT)

Principal Investigator: MAJ Patrick J. Woodman, MC

Department: OB/GYN, UG

Facility: MAMC

Associate Investigator(s): COL Gary D. Davis, MC; MAJ Ronald J. Place, MC; CPT Vanessa D. Dance, MC; COL Romeo P. Perez, MC; James M. Nelson

Start Date:  
9/28/1999

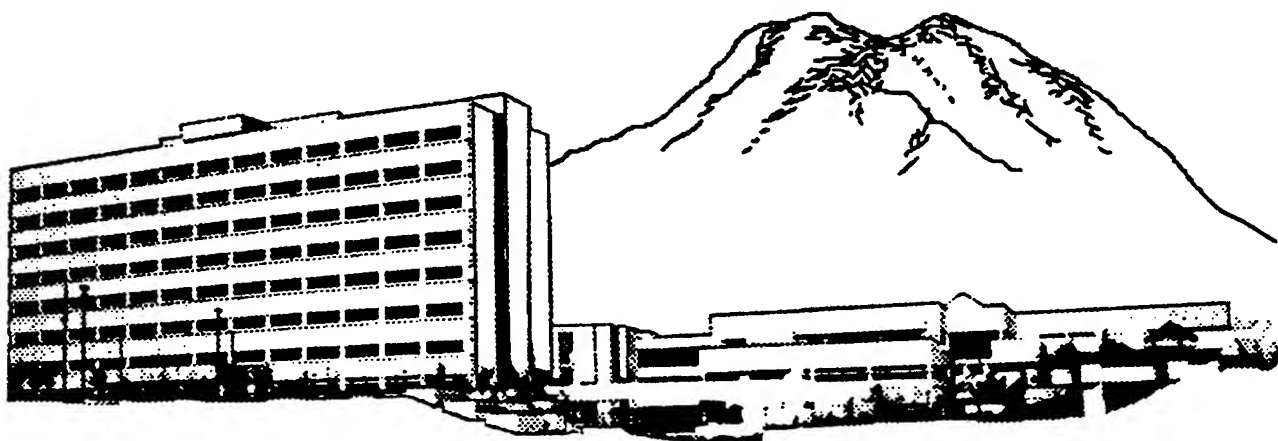
Est. Completion Date:  
Aug 00

Periodic Review:  
9/27/2000

**Study Objective:** To discover ways to prevent recognized and occult anal sphincter rupture and improve long-term primary closure outcome; thereby helping to prevent the development of future fecal and flatus incontinence.

**Technical Approach:** This study will investigate the occult anal sphincter disruption rate as a result of a variety of delivery types in primigravid women. The predominant method of episiotomy at MAMC is midline, which may affect the occult anal sphincter disruption rate. Primigravid women will be recruited from the OB/GYN clinic population and asked to participate postpartum. They will fill out a questionnaire, which will ask about their deliveries, their medical, surgical, colorectal histories and some randomization information. The investigator, who is blinded to the type of delivery, whether the patient had an episiotomy or tear, and other pertinent history, will perform an endoanal ultrasound of the anal musculature at approximately 6 weeks postpartum. Thickness and morphology of the internal and external sphincter and perineal body will be performed and recorded on a data sheet (attached). Those patients in which defects are found will be asked to return at approximately 6 months for repeat examination. At a later date, a second investigator will compare and verify the information requested in the patient questionnaire and obtain information about diagnoses, malposition, degree of episiotomy and extension, and labor augmentation. This will be recorded on the verification sheet. The patients will be identified by coded numbers, cross-classified to FMP/SS#. All data will be entered and analyzed using SPSS, Primer of Biostats, or similar statistical package. A small group of women (approximately 10) will be recruited to participate in an investigation on how the anal sphincter musculature morphology changes during the three trimesters of pregnancy. Each woman will undergo a series of three anal ultrasonographic examinations, one per trimester. These subjects would also the patient questionnaire, and the same data points would be obtained: Thickness and morphology of the internal and external anal sphincter and the perineal body. At the end of the trial, each woman will be asked if she would like to continue with the main study protocol, which would require a separate consent form.

**Progress:** During continuing review, the PI requested this protocol be suspended pending a possible change in study methods. Work on this study has not been initiated at MAMC.



## Detail Summary Sheets

Department of Pathology

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/134

**Status:** Ongoing

**Title:** Detection of Genotypic/Phenotypic Abnormalities in the Mucosal Lymphoid Tissue of Celiac Disease

**Principal Investigator:** CPT Jeffrey A. Vos, MC

**Department:** Pathology

**Facility:** MAMC

**Associate Investigator(s):** James E. Coad, M.D.; LTC Mark D. Brissette, MC; LTC Jerome B. Myers, MC

**Start Date:**  
9/26/2000

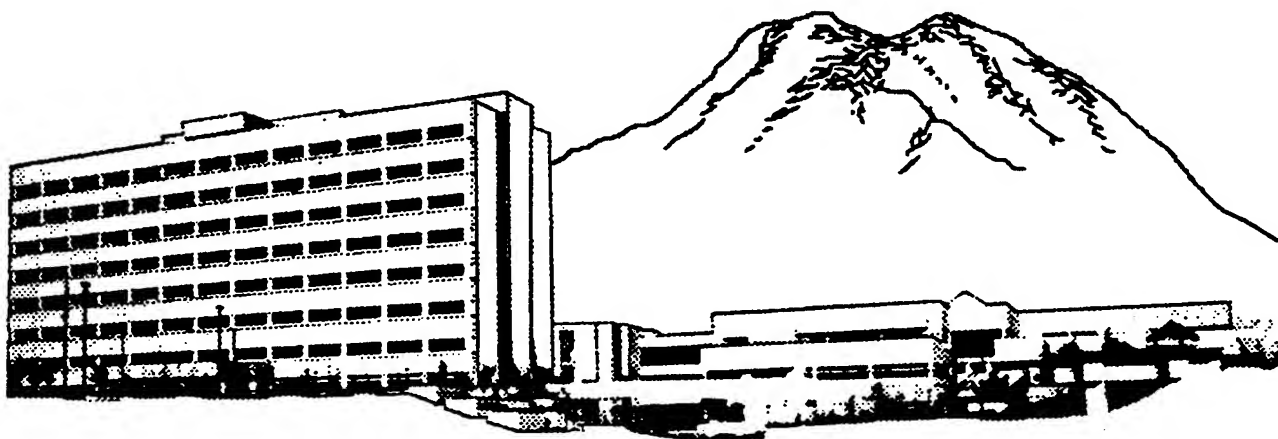
**Est. Completion Date:**  
Dec 00

**Periodic Review:**  
N/A

**Study Objective:** To determine if immunophenotypic aberrations and/or clonality (findings that would suggest the presence of a low grade lymphoma) can be identified in the T lymphocytes of small bowel biopsies of patients with celiac disease.

**Technical Approach:** This retrospective, descriptive study will look at paraffin-embedded tissue blocks from patients who have had duodenal biopsies with a histologic interpretation of "celiac sprue" or "changes consistent with celiac sprue". Biopsied tissues from the confirmed "celiac sprue" subjects will be compared to normal tissues by doing an immunohistochemical analysis and a T cell gene rearrangement analysis. Conclusions may be used to help establish markers for the detection of low-grade malignant conditions in celiac disease.

**Progress:** Data collection for this protocol has commenced on three "normal" small bowel specimens that have been assessed at MAMC. Additionally, 15 suitable study specimens of celiac material have been identified from MAMC archival material. No data analyses have been performed to date.



## Detail Summary Sheets

Department of Pediatrics



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/056	<b>Status:</b> Completed
<b>Title:</b> A Survey to Determine the Safety and Efficacy of Continuous Intrathecal Baclofen Infusion in Children and Adolescents with Spasticity of Cerebral Origin		
<b>Principal Investigator:</b> Lt Col William M. Campbell, USAF		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL William O. Walker, Jr., MC		
<b>Start Date:</b> 3/28/2000	<b>Est. Completion Date:</b> Jun 00	<b>Periodic Review:</b> N/A

**Study Objective:** Report on the long-term safety and efficacy of CITB in children and adolescents with spasticity of cerebral origin.

**Technical Approach:** Retrospective review of collected data in patient files and computer database; prospective telephone survey.

**Progress:** 21 consecutive children and adolescents who began CITB at Children's Hospital and Regional Medical Center (CHRMC), Seattle, between Dec 94 and Dec 98 were included. At the time of implant, 19 recipients had spastic quadriplegia and two had spastic diplegia. 13 had detectable athetosis or dystonia as a secondary component of their disorder. 14 children had Level V (most severe) impairment and seven children had Level IV impairment. Median age was 12 years at the time of pump implantation.

**Conclusions:** Continuous intrathecal baclofen infusion (CITB) appears to be effective in reducing spasticity of cerebral origin in children and adolescents. It does not appear to result in functional improvements on the Gross Motor Function Measure or Pediatric Evaluation of Disability Inventory in children with GMFCS Level IV and V severity. These outcome measures may not be sensitive to important changes in severely involved children. By family and patient report, this treatment appears to improve comfort, reduce pain, improve ease of care, and improve functional independence.

Adverse events are common, but are often related to preexisting problems. The treatment itself might predispose some recipients to decubiti or other adverse events. The role of CITB in the occurrence of pancreatitis in two recipients is unclear. It is implausible that pancreatitis could be caused by intrathecal administration of baclofen but not by oral administration. The oral dosage is approximately one hundred times greater and yield measurable blood levels while intrathecal administration does not lead to detectable levels in blood. However, there still might possibly be a causal relationship between acute pancreatitis and the pump implantation procedure and/or subsequent anatomic or postural changes. These observations may have important implications for establishing patient selection criteria and treatment goals, improving patient follow-up, and developing strategies to prevent and manage adverse events.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/042	<b>Status:</b> Ongoing
<b>Title:</b> Does Breast-feeding Decrease Amount of Antibiotics or the Exposure to Second and Third Line Antibiotics in Infants Less Than a Year of Age?			
<b>Principal Investigator:</b> LTC Mary P. Fairchok, MC			
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Michelle S. Flores, MC			
<b>Start Date:</b> 2/22/2000	<b>Est. Completion Date:</b> Feb 01		<b>Periodic Review:</b> N/A

**Study Objective:** To determine if breast-feeding in infancy decreases the amount of antibiotics prescribed or number of second and third line antibiotics prescribed in the first year of life.

**Technical Approach:** This study will gather information on healthy infants and whether or not the mode of feeding (breast versus bottle) has any effect upon the number of days on antibiotics or the use of second and third-line antibiotics. A preliminary pilot will be done to determine sample size. At the 6 month and 12 month well child visits parents will be questioned as to modes of feeding and use of antibiotics. Other possible confounding variables will also be assessed to include daycare use and smoking. CHCS will then be searched for antibiotics prescribed and charts will be reviewed for any emergency room or spectrum clinic visits. Infants will be compared at the 6 month and 12 month periods, and chi square tests will be used to determine if differences in number of days of antibiotics are significant. In addition, the types of antibiotics will be recorded to determine if mode of feeding affects the number of second and third-line antibiotics prescribed. Infants will be grouped into exclusively breast fed (less than one bottle per day for greater than or equal to 13 weeks), exclusively bottle fed (no breast feeding), and partially breast-fed (termination of breast-feeding prior to 13 weeks and initiation of bottle feeding or any combination of breast-feeding and bottle). Antibiotic use will be determined via reviewing the CHCS system and number of days and type of antibiotic prescribed will be recorded. In addition, charts will be used to look for any antibiotic use which may have been prescribed via the emergency room or spectrum clinic since these often are not entered into the CHCS system. Charts will also be randomly reviewed to determine if parental recall is reliable. Groups will be compared statistically at the 6 month period and 12 mos. Comparisons of number of days on antibiotics and number of second and third line antibiotics will be made between groups using chi-square. ANOVA analysis will then be used to assess affects of confounding variables such as daycare use and smoking. A preliminary pilot prior to initiation of study will be done with about 30 subjects for purposes of determining what amount of days and what sample size will be necessary for statistical significance with p values less than 0.05. Sample size will then be determined and study will be adjusted as necessary.

**Progress:** 356 subjects have been entered in this study in FY00. Data collection is complete and data analysis is planned to begin in December. This study is closed to further enrollment.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 90/092

**Status:** Ongoing

**Title:** Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses

**Principal Investigator:** LTC Mary P. Fairchok, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** COL James S. Rawlings, MC; MAJ Thomas A. Perkins, MC; LTC Joanna C. Beachy, MC; COL Marvin S. Krober, MC

**Start Date:**  
7/20/1990

**Est. Completion Date:**  
Sep 91

**Periodic Review:**  
7/25/2000

**Study Objective:** To analyze laboratory assays for detection of HIV infection in children and to correlate the results with the clinical status of the child.

**Technical Approach:** Technical Approach: This will be a multicenter study funded by Walter Reed Army Medical Center. The plan of this protocol is to evaluate the usefulness of new assays as they are developed, using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard HIV testing using those tests that are most developed. Surplus will be utilized for less well developed assays or stored for future analysis. Results from the tests will be compared to conventional assays used to diagnose adult HIV infection, such as ELISA, western blot, and culture, to determine their usefulness in children. These specimens will also be used to develop improvements and new methods for HIV testing in children. This analysis will be done in 120-150 individuals at three month intervals to determine if changes in these tests correlate with changes in the patient's clinical or immunological status. Most of the data generated in this protocol will be qualitative and will be correlated to quantitative clinical data using Spearman's Rank Correlation. Logistic regression will be used for correlating the numerical data to noncontinuous clinical measures. Analysis of data from different clinical groups (patients who remain asymptomatic versus those who develop AIDS) will be compared using two-way ANOVA to determine significant differences between clinical groups.

**Progress:** No patients were enrolled in FY 2000. This protocol remains open to patient enrollment.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/118      **Status:** Ongoing

**Title:** The Efficacy of Duct Tape versus Cryotherapy in the Treatment of Verruca vulgaris (the common wart)

**Principal Investigator:** CPT Dean Focht, MC

**Department:** Pediatrics      **Facility:** MAMC

**Associate Investigator(s):** LTC Mary P. Fairchok, MC; Carole A. Spicer

Start Date:	Est. Completion Date:	Periodic Review:
8/22/2000	July 01	N/A

**Study Objective:** To determine if application of duct tape is an effective treatment of common warts in comparison to standard treatment with cryotherapy.

**Technical Approach:** This study will enroll approximately 100 subjects to one of two treatment arms: cryotherapy or duct tape. Subjects who receive cryotherapy will have their warts frozen and be instructed to debride the wart between visits. The subjects will return every two weeks to assess progress and receive further cryotherapy. If the wart is not gone within four months, subjects will be referred to dermatology for further treatment.

The duct tape will be applied in the clinic and left on for six days at which time the tape will be removed and the wart debrided. The next morning, duct tape will once again be applied to the wart. Cryotherapy will be initiated in the clinic and if the wart is not gone in four months, the subject will be referred to dermatology. Results will be compared to assess relative efficacies.

**Progress:** This study recently received final IRB approval. No work has been initiated on this study in FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/072

**Status:** Completed

**Title:** Neonatal Screening in the DoD: Ethnic Distribution of Genetic Risk in the Military Health System Should Determine Screening Protocol Not State Lines

**Principal Investigator:** COL Roderick F. Hume, MC

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** Laura S. Martin, M.D.; MAJ Wanda A. Barfield, MC; COL(ret) Robert V. Jarrett, MC; LTC(ret) Deb Divelbiss, RN; COL Patrick C. Kelly, MC; James Birkenbaugh, MD; CPT Mark E. McGranahan, MC

**Start Date:**  
3/28/2000

**Est. Completion Date:**  
Mar 00

**Periodic Review:**  
N/A

**Study Objective:** To determine a Military Health Systemwide pathway for neonatal screening which would simplify the process, lessen unintended risk and enhance the cost effectiveness of neonatal screening in the Department of Defense.

**Technical Approach:** First phase: assessment of current state of the art regarding neonatal screening and therapeutic outcomes. Given the ethnic driven risk distribution for specific diseases, the MHS data set will be used to determine the DoD Beneficiary Risk Profile, compare Regions within the DoD, and between the States and Regions.

**Progress:** All US Military Health System eligible births for 1996 (n=67,894) were evaluated. Data was analyzed regarding location of birth, race and gender, and information compiled regarding metabolic and endocrinologic disorders screened in newborns at DoD Regional Medical Centers. Results: DoD births differed from the civilian sector in ethnicity but not in gender. DoD populations had a greater percentage of African-Americans, White, and Hispanic births. All DoD neonates received screening for hypothyroidism and phenylketonuria. All other tests were screened at the discretion of each state, with no relationship between the cost of screening and the number of conditions screened. Conclusions: Based on preliminary findings, this study recommends that DoD newborn screening be based on ethnic distribution and genetic risk, not state or region of birth. Disorders that should be screened include Biotinidase Deficiency, Congenital Adrenal Hyperplasia, Galactosemia, Amino Acid Disorders (MSUD and PKU) Congenital Hypothyroidism, Hemoglobinopathies, Cystic Fibrosis, Medium Chain Acyl-Co A Dehydrogenase Deficiency and Glutaric Acidemia type 1. An algorithm for newborn screening in the DoD was devised to include term and premature newborns, which encompasses early discharge, family PCS moves, and DoD eligibility changes. Finally, this study recommends benchmark qualities of an appropriate facility, which include centrality, extensive experience, administrative support, genetic consultation, and web-based reporting systems. If cost-effective, the program should be disseminated throughout the DoD.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 97/056      **Status:** Completed

**Title:** Physiological and Feeding Effects of Neonatal Physical Therapy Procedures on Preterm Infants in a Neonatal Intensive Care Unit Setting

**Principal Investigator:** Jane K. Sweeney, Ph.D., PT, PCS

**Department:** Pediatrics

**Facility:** MAMC

**Associate Investigator(s):** MAJ Roger M. Hinson, MC; MAJ Wanda A. Barfield, MC

**Start Date:**  
2/21/1997

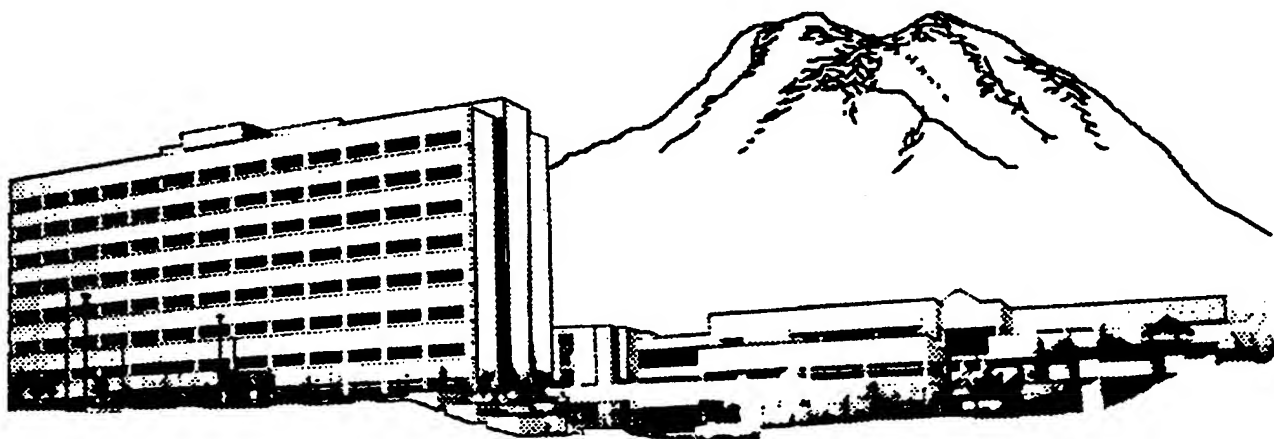
**Est. Completion Date:**  
Oct 99

**Periodic Review:**  
2/22/2000

**Study Objective:** (1) To study and compare the physiological tolerance of medically stable, preterm infants to two interventions: neonatal hydrotherapy and a control intervention of no physical handling or social stimulation, (2) to evaluate and compare the effects of neonatal hydrotherapy in a control condition of no handling or social stimulation on oral feeding performance in medically stable, preterm infants.

**Technical Approach:** This is a within subject, randomized cross over design for treatment (hydrotherapy) and control (rest period) condition. 30 medically stable, preterm infants (31 to 35 weeks post-conception) in a neonatal intensive care unit setting. After an 10 minute initial baseline phase, subjects are randomly assigned to a physical therapy intervention followed by oral feeding and concluded by a 10 minute recovery baseline phase. The intervention conditions are a 15 minute session of neonatal hydrotherapy or a control condition of no handling. The physiological measures of heart rate, respiratory rate, mean arterial pressure, temperature, intracranial pressure, and oxygen saturation are recorded continuously and will be compared across intervention groups among the four phases of the study using a repeated measures analysis of variance. Feeding performance of volume ingested and duration of feeding will be compared between two infant groups and analyzed using ANOVA.

**Progress:** 40 subjects have been enrolled in this study (9 for a pilot study, 31 for data collection). No further subject enrollment will be conducted. Data collection is complete, and data analysis is in progress; however no conclusions are available at this time.



## Detail Summary Sheets

Department of Pharmacy

### Detail Summary Sheet

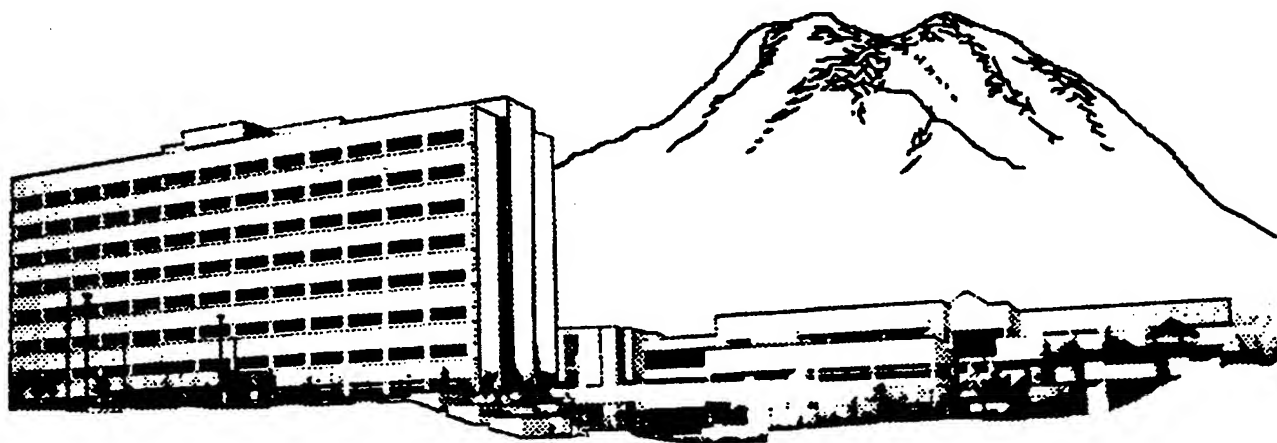
<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/106	<b>Status:</b> Completed
<b>Title:</b> Pilot Study to Determine the Effectiveness of Glutamine in the Treatment of Paclitaxel Induced Myalgia, Arthralgia and Neuropathy		
<b>Principal Investigator:</b> COL Dennis R. Beaudoin, MS		
<b>Department:</b> Pharmacy	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ David E. McCune, MC; MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 9/28/1999	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the efficacy of glutamine in treating the common, non-hematological, dose-limiting toxicities (myalgia, arthralgia and neuropathy) associated with the use of paclitaxel.

**Technical Approach:** All patients receiving paclitaxel (doses  $\geq 135$  mg/M<sup>2</sup> will be asked to participate in the study. Those consenting will be provided pain scales (arthralgia / myalgia / neuropathy) and counseled how to complete them prior to their first paclitaxel dose. Patients reporting arthralgia, myalgia or neuropathy will be provided glutamine at time of next paclitaxel dose. Post treatment pain scales completed by the patient will then be collected. Comparison of pre and post treatment observations will be completed to determine if glutamine was effective in relieving paclitaxel induced toxicities (arthralgia / myalgia / neuropathy).

**Progress:** Twenty patients were enrolled in this study at MAMC. Seven patients met the study criteria and were evaluated. There was a clinically and statistically significant decrease in myopathy and overall pain during cycle 2 ( $p=0.0355$  and  $p=0.200$  respectively) for patients receiving glutamine. There was no statistically significant difference in arthropathy and neuropathy. Conclusions indicate glutamine is effective in reducing paclitaxel-induced myopathy. Due to the small sample size a clinically significant difference could not be determined in arthralgia and neuropathy. This pilot study demonstrates the need for multicenter double-blind randomized clinical trials to determine the effectiveness of glutamine in reducing or preventing paclitaxel-induced toxicity.





## **Detail Summary Sheets**

Physical Therapy,  
Physical Medicine & Rehabilitation Service

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 98/030      **Status:** Ongoing

**Title:** Physical Therapy Treatment Effectiveness for Osteoarthritis of the Knee: A Prospective, Randomized, Controlled Comparison of Supervised Clinical Exercise and Manual Therapy Procedures versus A Home Exercise Program

**Principal Investigator:** COL Nancy E. Henderson, SP

**Department:** PMRS/Physical Therapy      **Facility:** MAMC

**Associate Investigator(s):** COL Gail Deyle, SP; MAJ Robert L. Matekel, SP; Skyeann Allison; MAJ Jeremy Hutton, SP; CPT John Stang, SP; CPT David Gohdes, SP; CPT Mike Ryder, SP; CPT Matt Garber, SP

**Start Date:**  
12/18/1997

**Est. Completion Date:**  
Oct 98

**Periodic Review:**  
3/28/2000

**Study Objective:** To evaluate the effectiveness of manual physical therapy treatment for osteoarthritis of the knee compared to a home exercise program.

**Technical Approach:** Subjects will be randomly assigned to one of two treatment groups. Subjects will undergo a thorough clinical examination by the treating physical therapists and then turned over to a trained research assistant (tester) blinded to the group assignment. The tester will obtain measurements of the dependent variables using the Wester Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and a six-minute walk test. The subjects will be returned to the treating therapist and treatment will begin as per group assignment

Group 1 will perform an in-clinic series of closely supervised exercises. Subjects will also receive manual physical therapy as indicated by examination and do home based exercise on the days when they are not in clinic. At the end of eight sessions the subject will be retested with the tester 2 days after the last exercise session and at the same time of day as the pretest

Group 2 will receive a home based exercise program, instructed to the subject by the treating physical therapist, and a detailed supporting handout and compliance log. Subjects will return to the clinic 2 weeks later to ensure proper execution of the exercises and compliance with the program. After completing 4 weeks the subject will be retested with the tester 2 days after the last exercise session and at the same time of day as the pretest.

**Progress:** No new subjects were enrolled onto this protocol during FY 2000. The total number enrolled remains at 37. Four subjects have reached the "one year mark" in the study and have been retested. Three more subjects have yet to be tested. Data will be combined with that from other sites and then analyzed. No data analysis is available at this time.

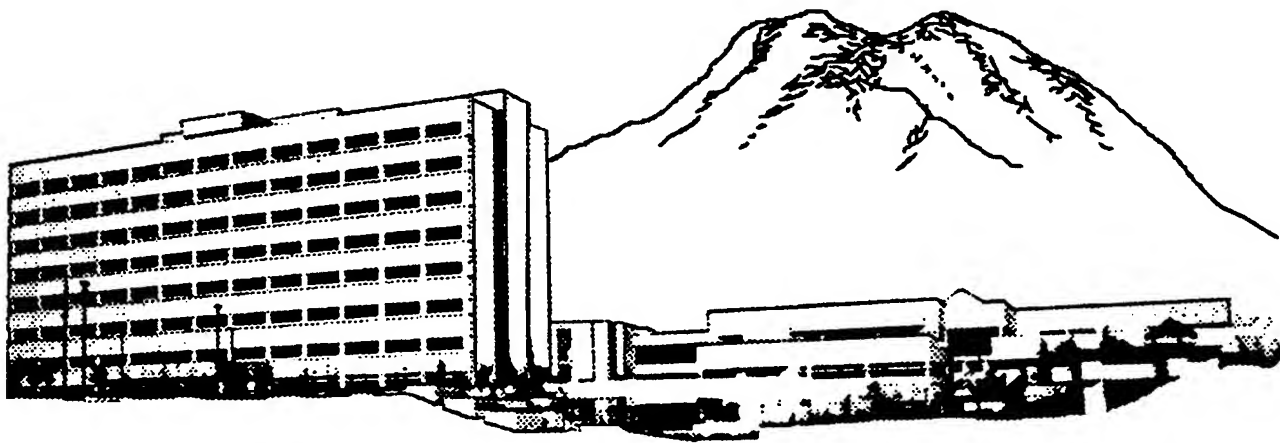
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/027	<b>Status:</b> Suspended
<b>Title:</b> Mandatory Physical Training and Physical Readiness in Postpartum Soldiers		
<b>Principal Investigator:</b> COL Nancy E. Henderson, SP		
<b>Department:</b> PMRS/Physical Therapy	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Roderick F. Hume, MC; CPT Mary C. Adams, MC		
<b>Start Date:</b> 1/26/1999	<b>Est. Completion Date:</b> Jan 02	<b>Periodic Review:</b> 3/28/2000

**Study Objective:** (1) To compare the proportion of MPPPT trained soldiers who pass the Army Physical Fitness and body-fat standards at 6 and 12 months postpartum to the proportion of non-pregnant controls who pass during the same time interval, (2) to compare injury rates in MPPPT trained soldiers during the postpartum period to the injury rates in non-pregnant controls during the same time intervals, (3) to compare postpartum fitness, body-fat and injury rates in MPPPT trained soldiers to postpartum soldiers exempt from MPPPT and (4) to compare postpartum fitness, body-fat and injury rates in MPPPT trained soldiers to non-MPPPT trained postpartum soldiers (an historical control).

**Technical Approach:** Subjects will be scheduled for 3 appointments during this one year study; day 1, 6 months and one year. At each appointment body composition will be measured and subjects will be asked to complete a questionnaire, to include questions about age, ethnic background and exercise patterns. Medical records will be reviewed for injuries or illness. PT scores from the last PT test taken and from the next 2 PT tests will be recorded.

**Progress:** This protocol remains suspended pending funding.



**Detail Summary Sheets**  
Preventive Medicine Service

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/012	<b>Status:</b> Ongoing
<b>Title:</b> Noninvasive Measurement of the Surface Radiation Dose of Nuclear Medicine Patients Utilizing Thermal Luminescent Dosimeters (TLD)			
<b>Principal Investigator:</b> LTC Mark W. Bower, MS			
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Scott Hudson; MAJ Stacia L. Spridgen, MS			
<b>Start Date:</b> 10/26/1999	<b>Est. Completion Date:</b> Apr 00		<b>Periodic Review:</b> N/A

**Study Objective:** Determine the response of thermoluminescent dosimeters (TLD) on the surface of personnel undergoing typical Nuclear Medicine procedures at positions where occupational radiation dose measuring TLD are normally worn.

**Technical Approach:** Patients referred to Nuclear Medicine as part of their normal medical care will be given one to two small thermoluminescent dosimeters (TLD) at the time of their injection and will be asked to wear them in designated locations; at the hip, collar or breast pocket. The amount of time the TLD is worn will be recorded. The TLD response from patients undergoing similar nuclear medicine procedures will be correlated to determine an average response for that procedure and then compared to the calculated TEDE. Correlation will also be made between the symptomatic and non-symptomatic patients.

**Progress:** Dosimeters have been given to five patients and sent off for analysis. Results were not available at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/004	<b>Status:</b> Completed
<b>Title:</b> Vaccinating U.S. Army Soldiers Against Lyme Disease: A Cost-Effectiveness Analysis		
<b>Principal Investigator:</b> CPT Arthur B. Cajigal, MC		
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Jeffrey D. Gunzenhauser, MC		

**Start Date:**  
10/26/1999

**Est. Completion Date:**  
Dec 99

**Periodic Review:**  
N/A

**Study Objective:** To evaluate economic and clinical outcomes of a program of routine vaccination against Lyme disease.

**Technical Approach:** This study will use Decision Analysis (software) to model, via Markov process, the estimated cost per case prevented and cost per QALY gained.

**Progress:** The cost-effectiveness of vaccination to prevent Lyme disease was evaluated using the decision analysis method in a hypothetical cohort of 100,000 U.S. Army soldiers. Cost effectiveness was measured as the cost per case prevented and as the cost per quality of life year (QALY) gained. Baseline assumptions included: annual disease incidence of 0.1%, cost of vaccine and administration of \$70, and vaccine efficacy of 71%. Sensitivity analyses of all key parameters were performed. Results showed the cost per case of disease prevented was in excess of \$50,000 among soldiers with an annual disease risk of 0.1%. The cost per QALY gained was in excess of \$1 million. When the disease incidence approached 1% per year (a rate far below recent military experience), the costs were \$7,000 per case of Lyme disease prevented and \$90,000 per QALY gained. Outcomes were most sensitive to annual Lyme disease incidence. Conclusions: The cost of selective vaccination of US Army soldiers to prevent Lyme disease is excessive when compared to other vaccine-preventable diseases. Therefore, using vaccine to prevent Lyme disease is currently not cost-effective

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**Conclusion:** The cost of selective vaccination of U.S. Army soldiers to prevent Lyme disease is excessive when compared to other vaccine-preventable diseases. Using vaccine to prevent Lyme disease is not currently cost-effective.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/076	<b>Status:</b> Completed
<b>Title:</b> Immune Response to Community-Acquired Campylobacter jejuni Infection in United States Military Personnel on Deployment in Korat, Thailand (Cobra Gold 99)		
<b>Principal Investigator:</b> COL James E. Cook, MC		
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> D Tribble		
<b>Start Date:</b> 6/22/1999	<b>Est. Completion Date:</b> Aug 99	<b>Periodic Review:</b> N/A

**Study Objective:** 1) Characterize the immune response to community-acquired *C. jejuni* infection in U.S. military personnel deployed to Korat, Thailand during Cobra Gold 99. 2) Compare the ranges of immune response found in community-acquired and experimental *C. jejuni* infections.

**Technical Approach:** Volunteer enrollment will occur at the 47th Combat Support Hospital in Korat during the period of the Cobra Gold 99 exercise (May 10-30). Stool and blood samples will be processed and stored in the field laboratory in Korat and transported to AFRIMS and NNMC for analysis at exercise completion. Stool specimens will be cultured and bacterial diarrheal pathogens will be presumptively identified in the field laboratory in Korat. Further evaluation will be completed at AFRIMS. All *C. jejuni* isolates will be archived and transported to NMRC. Post-deployment blood specimen collection (during July 1999) for enrolled volunteers will occur at both Ft. Lewis, Washington and Schofield Barracks in Hawaii with on-site processing prior to transport to NMRC.

**Progress:** A total of 110 patients who presented with acute diarrhea were enrolled during the 14-day in-theater period. A valid assessment of the percent enrollment for patients presenting with acute diarrhea is available for the May 8-16 period (prior personnel and their assigned BAS deploying to the field). During this period, enrollment into the study was occurring at a minimum rate of 84%. The reason this is a "minimum rate" is that a patient presenting with the chief complaint of diarrhea and not enrolled were often not eligible due to not meeting the acute diarrhea definition. Peak enrollment rates occurred in the 2nd week of the exercise consistent with observed peak rates in the DNBI (disease non-battle injury) data

**Summary of results obtained:** The observed diarrheal illness covered a spectrum of clinical syndromes including watery diarrhea (78%), predominately vomiting illness with diarrhea (7%), and dysentery (15%). The coexistence of fevers was observed in 50-69% of the patients irrespective of the presenting clinical syndrome. Approximately one-fourth of the patients were either admitted or placed in quarters. The number of patients returned to duty, 74%, tends to understate the affect the illness had on the soldier's functional abilities since many of the personnel were able to greatly limit their activities despite duty status. A more correct representation of the illness' impact on function is the daily global assessment by the volunteers during follow-up. Using these reports, a return to normal function was not rapid for many patients, with 47% still reporting dysfunction after 48 hours despite receiving treatment

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/090

**Status:** Ongoing

**Title:** Development of an ADS-based Syndromic Surveillance System Using Sexually Transmitted Diseases as a Prototypic Sentinel Condition

**Principal Investigator:** COL Jeffrey D. Gunzenhauser, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** COL Kelly T. McKee, Jr., MC; CDR Randy Culpepper, MC (Navy)

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
July 01

**Periodic Review:**  
N/A

**Study Objective:** (1) To build an interface between the Ambulatory Data System (ADS) and a Geographic Information System (GIS) by linking these systems to extract information on outpatient Sexually Transmitted Diseases from 2 geographically distinct Army installations: Fort Bragg, NC, and Fort Lewis, WA, and (2) To verify ADS diagnoses reported through CEIS by linkage with laboratory data on tests performed to diagnose syphilis, gonorrhea, and chlamydia contained in CHCS at Madigan Army Medical Center.

**Technical Approach:** This is an observational study using existing data from two sources: CEIS (ADS) and CHCS. The overall goal is to develop a prototypic syndromic system which links CEIS data and a GIS software system AND to assess the accuracy of diagnoses of STDs (gonorrhea, syphilis, and chlamydia) reported through CEIS. Accuracy will be assessed by merging data retrieved from CEIS with lab-confirmed diagnoses stored in the Madigan CHCS system.

The study population is any Madigan beneficiary who had a lab test performed for an acute STD syndrome (syphilis, gonorrhea, or chlamydia), who had an ICD-9 diagnosis for an acute STD syndrome (same) recorded in CEIS via ADS, or both. The study period is 1 Jan 97 through 31 Dec 99. To ensure that lab tests or clinic visits occurring on the margins of the study period are identified and included, data will actually be collected for the period Dec 1996 through January 2000, but will eventually be truncated to delete information on any beneficiaries for whom BOTH the lab test and the clinic visit occurred outside of the study period. Beneficiaries for whom at least one of these events occurred within the study period will be included in the analysis.

Patients with ADS-based diagnoses of syphilis, gonorrhea, and chlamydia occurring during the study period will be identified in central CEIS data files by one of the research collaborators. Information extracted from CEIS will include FMP, SSN, date of birth, clinic visit location, date of clinic visit, and ICD-9 coded diagnosis. Patients with diagnoses of syphilis, gonorrhea, and chlamydia occurring during the study period will be extracted from the Madigan CHCS system by the principal investigator using the ad hoc query. Information extracted from CHCS will include FMP, SSN, gender, date of birth, address of beneficiary (street address, city, state, and ZIP code), date of lab test, lab test result, and MEPRS code of the clinic (medical resource center) at which the test was ordered.

These two data acquisition efforts will identify all persons with a positive laboratory diagnosis for an acute STD syndrome, a positive ICD-9 diagnosis for the same acute STD syndromes, or both. However, because the primary analytic technique of the study will be McNemar's 2x2 table, information will also be needed on beneficiaries who had both a negative lab test and an ADS-based ICD-9 diagnosis for a condition other than an acute STD syndrome. To complete this cell of the 2x2 table, patients at Madigan who had a negative test for syphilis (RPR/VDRL), gonorrhea (culture or GenProbe), or chlamydia (Chlamydiazyme or GenProbe) during the study period will be identified. Their SSNs and FMPs will be collected in a data set and sent to associate investigator to batch merge with CEIS to identify ICD-9 codes resulting from clinic visits during which these diagnostic tests were performed. The merging of these two data sources will in this way identify persons for whom both a CHCS-recorded test was performed and an ICD-9 code was entered in ADS from the related clinic visit, both of which are NEGATIVE for a diagnosis of an acute STD.



This approach is exhaustive in identifying all persons who fit these criteria during the study period.

The study method described will require that personally identifying information must be shared between investigators on the East Coast and at Madigan. Specifically, information on patients with positive diagnosis for acute STD syndromes will need to be sent from the CEIS extraction origin to the investigator at Madigan to validate whether or not a lab test was performed and what the result was. Similarly, personal identifiers on all Madigan patients for whom a diagnostic test for an acute STD syndrome is recorded in CHCS will need to be sent to the CEIS POC to ascertain whether an encounter was documented in ADS (CEIS) and whether a diagnosis of an acute STD syndrome was recorded.

To protect privacy, efforts will be made to safeguard data. Names of beneficiaries will not be abstracted from either source. Family Member Prefix (FMP) coupled with the sponsor Social Security Number (SSN) will serve as the means of record linkage. Once all data has been collected, data from the two sources (CEIS and CHCS) will be merged (by FMP and SSN). Dates of birth will be converted to ages. After merging and age conversion, FMPS, SSNs, and DOBs will be eliminated from the data set. Address information will be maintained, however, to allow for precise mapping of beneficiary residence. If the GIS program purchased for this study is unable to use specific street address information, this field will be deleted, and only city, state and zip code information will be maintained in the final data set used for analysis. Geographic information data usable in a GIS system (ArcView or comparable software) will be purchased or downloaded from the Internet. Clinical data will be merged into the GIS to plot frequencies of specific diagnoses by Zip Code, SMSA, or county of residence, as the GIS software will allow.

**Progress:** Work has not yet been initiated on this study at MAMC during FY00. Primary data collection for this study is expected to occur between November 2000 and February 2001. This collaborative study, involving researchers at USAMRIID and their contractors, continues to negotiate a number of non-science related administrative requirements.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/092	<b>Status:</b> Ongoing
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**Title:** Outpatient Morbidity Study of ROTC Cadets During Advanced Camp

**Principal Investigator:** COL Jeffrey D. Gunzenhauser, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** LTC Gregory A. McKee, MS

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Oct 00

**Periodic Review:**  
N/A

**Study Objective:** To estimate incidence rates of outpatient morbidity experienced by Cadets participating in Advanced ROTC Camp at Ft. Lewis, WA and to associate the occurrence of various medical conditions with various phases of the Advanced ROTC Camp.

**Technical Approach:** This observational study will look at medical records and personnel rosters compared to training schedules for cadets in ROTC Advanced Camp. Medically reported incidents will be divided up according to how many "person-days" are spent at each part of camp. This study will analyze what sort of injuries and illnesses are associated with various stages of the ROTC Advanced Camp.

**Progress:** Data collection has been completed. This study is currently in the data entry/analysis phase. Final analyses are expected in Spring 2001.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/033

**Status:** Ongoing

**Title:** Breast Cancer Risk Assessment Among Women Beneficiaries Eligible for Medical Care in the Pacific Northwest, Region 11

**Principal Investigator:** COL Jeffrey D. Gunzenhauser, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** MAJ Heidi P. Terrio, MC; Troy H. Patience, B.S.

**Start Date:**  
2/23/1999

**Est. Completion Date:**  
Dec 99

**Periodic Review:**  
3/28/2000

**Study Objective:** To measure the prevalence of major breast cancer risk factors among female DOD beneficiaries in TRICARE Region 11, to estimate mammography usage rates among female beneficiaries in TRICARE Region 11 and to advise female beneficiaries that there is a genetics screening program available to all through the Breast Cancer Initiative in Region 11.

**Technical Approach:** 16,000 women beneficiaries will be mailed a one-page anonymous questionnaire on risk factors for breast cancer, and preventive screening prevalence with regard to self-breast exam, clinical breast exam and mammogram. Three mailings will be sent out in an effort to try and get a better than 70% response rate. All recipients of this questionnaire will be offered genetic counseling.

**Progress:** 7163 surveys were returned and data was entered. Overall mammography screening rates in the past two years for female beneficiaries in the prime screening age-group (50-70) approached 90%, which is excellent and far above the hypothesized level. Several aspects of the study are still under analysis, including specific analyses MTF and a Geographic Information System Analysis.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 200/078                      **Status:** Completed

**Title:** Soldiers on the Run, Running Shoe Use in Active Duty Soldiers at Ft. Lewis

**Principal Investigator:** CPT Mitchell Meyers, MC

**Department:** Preventive Medicine

**Facility:** MAMC

**Associate Investigator(s):** COL Jeffrey D. Gunzenhauser, MC

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Jun 00

**Periodic Review:**  
N/A

**Study Objective:** To evaluate soldier knowledge of proper running shoe selection and replacement, and to evaluate their actual purchasing, wear, and replacement of running shoes.

**Technical Approach:** This study will administer a survey to MAMC Companies in and around the time of APFT (relatively large number of female soldiers), soldiers inprocessing through Corporate Wellness (convenience sampling), and SF A-teams (large number of higher-ranking enlisted soldiers). Data will be verified from the APFT record if needed. Data from fully completed surveys will be entered into a MS Access file for initial analysis. Further analyses will be conducted after the resultant files are converted to an SPSS format.

**Progress:** A cross-sectional survey was administered to 148 males and 65 females from a US Army Medical Company. Five questions were asked to evaluate knowledge of key information necessary to assure consistent selection of appropriate running footwear. A five point scale was developed with one point given for each of the five questions that the subjects reported adequate knowledge. Five questions were to ascertain medical history of injuries associated with running. Mean results of these five running injury indicators were cross-tabulated with reported shoe selection knowledge levels and their relationships analyzed. The majority of AMEDD soldiers surveyed appeared to lack knowledge essential for the consistent selection of appropriate running shoes optimized for their training and biomechanical needs. Those with the lowest self-reported level of this knowledge were approximately twice as likely as those with the highest level of knowledge to experience past or current running related medical problems. Levels of knowledge were not statistically significant between males and females, but running injury indicators were consistently higher in women. These results suggest that education interventions could empower soldiers to choose optimized running shoes for themselves, which could result in a decrease in injuries related to running.

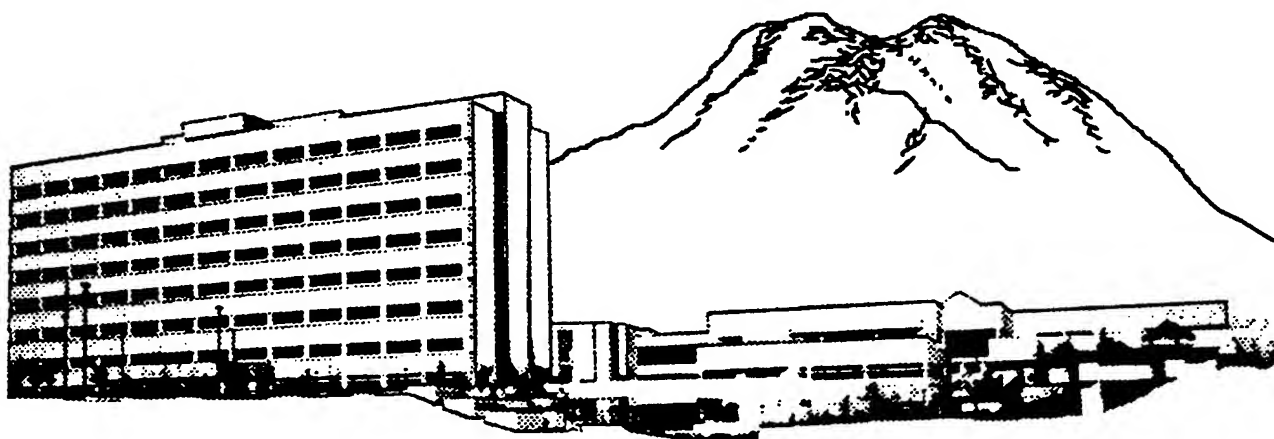
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/053	<b>Status:</b> Ongoing
<b>Title:</b> Using Readily Available Data to Monitor and Surveil Active Duty Injury Occurrence			
<b>Principal Investigator:</b> MAJ James S. Wadding, MC			
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC James D. Wells, MC; CPT Ryung Suh, MC; COL Jeffrey D. Gunzenhauser, MC			
<b>Start Date:</b> 3/28/2000	<b>Est. Completion Date:</b> May 00		<b>Periodic Review:</b> N/A

**Study Objective:** To determined if CHCS data can be used to predict loss of readiness due to injury and musculoskeletal illness (in the form of temporary profiles) and to aid in identifying problem areas and possible prevention opportunities on a recurring and real-time basis.

**Technical Approach:** This study is a pilot retrospective cohort study of the frequency and rates of key medical events related to injury occurrence in soldiers. A descriptive analysis of these events will provide thoughtful insight into the magnitude of morbidity typically severe enough to warrant lost-duty time. By looking at records of "sentinel" medications and clinic visits (entries in CHCS which predict the presence of injury or musculoskeletal illness) in CHCS) this study will evaluate the approximate lost time in a military population due to injury. Incidence of injury and illness will be verified by looking at the Standard Installation/Division Personnel Database (SIDPERS). Compiled data from random record selection will provide a profile of military readiness with regard to musculoskeletal injury and lost time due to injury.

**Progress:** This protocol had no work completed in FY00 due to time constraints. MAJ James Wadding has been IRB approved to assume the role of PI for this study, which remains ongoing.



## Detail Summary Sheets

Department of Psychology

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/105

**Status:** Ongoing

**Title:** Telemental Health / Electronic Neuropsychology (e-NP)

**Principal Investigator:** LTC Gregory Gahm, MS

**Department:** Psychology

**Facility:** MAMC

**Associate Investigator(s):** CPT Rhonda Koch, MS; LTC Bruce E Crow, MS; Dennis Kelly; Jack T. Norris

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jul 01

**Periodic Review:**  
N/A

**Study Objective:** (1) Evaluate ability of the ANAM2001, a computerized battery of cognitive assessment measures, to serve as a screening instrument for neuropsychological evaluations, (2) Establish infrastructure, procedures, and policies at MAMC to support an Army electronic neuropsychology service (e-NP), (3) Implement a secure server delivery platform for the ANAM2001 and demonstrate its functionality and (4) Explore the modification of ANAM2001 for true internet enabling.

**Technical Approach:** Patients who consent to participate in this study will, following their signing of the consent form, be assigned a case number. The case number will be input in place of the patient's name and SSN for all subsequent information gathering. Case system code will be consistent with the system under development at WRAMC for computerized neuropsychological reporting. This system identifies the test location, in this case MAMC, along with a new sequential 7 digit number. Thus the first subject would be MAMC0000001. Study subjects will complete a computerized history questionnaire containing pertinent questions regarding their background. Following completion of the questionnaire, a psychometrist (test administrator) will set the patient up with a series of automated neurocognitive measures (ANAM2001). Data from the automated measures will be transmitted to a secure server physically located within MAMC. Subjects will then be evaluated using the traditional neuropsychological evaluation measures utilized within the neuropsychological clinic.

**Progress:** No work on this study has been initiated during FY 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/109	<b>Status:</b> Ongoing
<b>Title:</b> Virtual Primary Care Clinic		
<b>Principal Investigator:</b> LTC Gregory Gahm, MS		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Jerald W. Rumph, MC; MAJ Nhan V. Do, MC; MAJ Robert B. Gibbons, MC; LTC Gary A. Wheeler, MC		
<b>Start Date:</b> 7/25/2000	<b>Est. Completion Date:</b> Mar 01	<b>Periodic Review:</b> N/A

**Study Objective:** (1) Develop an internet based primary care related service for implementation into the APCC, (2) Determine costs/feasibility of implementing functions as outlined in the original proposal and subsequent Statement of Work, and (3) Develop sub-protocol(s) for IRB approval for patient utilization study using the internet services with complete impact statements.

**Technical Approach:** This study will establish a prototype Virtual Clinic (VC) which will be designed to handle many of the administrative aspects of the APCC. Specific functional options for the VC will be documented and costs for development will be determined. The cost for the various options will be documented and decisions regarding function implementation will be made. A functional model will be operational by 01 January 2001, with data being gathered from January to March 2001. Information about subject interactions with the VC will be ready on the final reporting date of 05 March 2001.

**Progress:** This study received review and approval by MAMC IRB, CIRO and USAMRMC during FY00. Virtual Clinic development is progressing on schedule and will be ready for introduction at the beginning of January 2001.



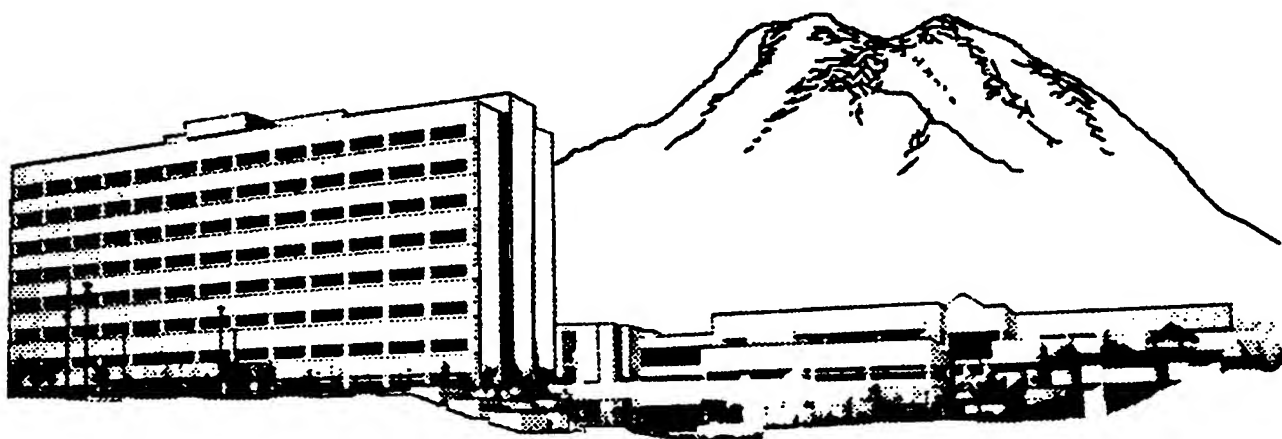
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/016	<b>Status:</b> Completed
<b>Title:</b> Prevalence of Anxiety Symptoms in General Pediatric and Specialty Pediatric Populations			
<b>Principal Investigator:</b> CPT Kathleen S. Lester, MS			
<b>Department:</b> Psychology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Kenneth A. Miles, MS			
<b>Start Date:</b> 1/26/1999		<b>Est. Completion Date:</b> May 99	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the rate of anxiety symptoms occurring among pediatric patients in a general population and in pediatric populations being evaluated/treated for asthma, GI complaints, neurologic disorders, diabetes and cancer.

**Technical Approach:** A valid and reliable instrument of self-report symptoms (Multidimensional Anxiety Scale for Children) will be given to pediatric patients with identified medical disorders of asthma, ADHD, diabetes, abdominal pain, headaches or cancer. Rates of anxiety symptoms within these medical populations will be ascertained and comparisons will be made between general and specialty populations as well as between medical subgroups. Correlation will be made between the medical subgroups with and without symptoms of anxiety and measure of medical utilization (number of clinic visits, ER visits and medications) and severity of illness.

**Progress:** This study was completed and the conclusions reported in the MAMC Annual Progress Report, FY 99.



## Detail Summary Sheets

Department of Radiology

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/088

**Status:** Ongoing

**Title:** Comparison of Computed Tomography Angiography and Digital Subtraction Angiography for the Pre-Operative Evaluation of Carotid Artery Disease

**Principal Investigator:** CPT David M. Keadle, MC

**Department:** Radiology

**Facility:** MAMC

**Associate Investigator(s):** CPT Christopher R. Spence, MC; MAJ Sean P. Murray, MC; MAJ Stephen M. Yoest, MC; James H. Timmons, MD; COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; Troy H. Patience, B.S.

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Jul 00

**Periodic Review:**  
7/25/2000

**Study Objective:** To evaluate the accuracy of Computed Tomography Angiography (CTA) in the evaluation of patients with atherosclerotic carotid artery disease. Comparison will be made with the with the accepted gold standard evaluation, digital subtraction angiography.

**Technical Approach:** The study sample will be obtained from consecutive patients who have had clinical evaluation and a duplex ultrasound examination in the vascular surgery clinic and who were referred for conventional angiographic examination of the carotid arteries. The plan is to evaluate 40 patients, although a preliminary statistical analysis will be performed after the first 20 patients to assure adequate sample size. Patients who agree to participate in the study will have CTA performed at least 72 hours prior the conventional angiography. These studies will be read by two radiologists. Conventional angiography will then be performed and will be read by two different radiologists. The physicians performing and reading the angiogram will be blinded to the results of the CTA study. Percent stenosis of the carotid artery will be computed using the North American Symptomatic Carotid Endarterectomy Trial method. The results of the CTA will be compared with the conventional angiogram using paired T-test analysis..

The CAT scan protocol used for the CTA exams is as follows: a non-contrast scan will be done first from the skull base to the aortic arch. These will be true axial images at 5 mm slice thickness and intervals using settings of 120 kV and 200 mA. Next, a contrast-enhanced study will be performed. 125 ml of non-ionic contrast material will be injected at a rate of 4ml per second. During the dynamic administration of this contrast material, a scan will be performed from the skull base to the aortic arch. These images will be acquired helically with a pitch of 2 and a slice thickness of 3 mm, and will use settings of 120 kV and 250 mA. These images will be reconstructed at 1 mm thickness, and will be reformatted in sagittal and coronal planes. In addition, 3 dimensional and maximum intensity projection (MIP) images will be obtained. The projected CT weighted dose (weighted 2/3 peripherally and 1/3 centrally) is 9.78 mGy for the contrast scan and 14.76 mGy for the non-contrast scan.

If the ultrasound and the CTA show only unilateral disease, the angiogram on the contralateral side will be abbreviated and will consist of only one contrast run as opposed to three. This will decrease the catheter time in that artery, which is suspected to decrease the chance of stroke. In addition, the decrease in radiation from excluding the two runs will likely exceed the extra radiation from the CTA.

**Progress:** To date, 17 subjects have been enrolled in the study at MAMC. Preliminary data evaluations are planned once 20 subjects have been enrolled, to determine the final number of subjects required to complete the study.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/085	<b>Status:</b> Ongoing
<b>Title:</b> Radiographic and Clinical Correlation of the Outcome of Calcaneal Osteotomy for Talocalcaneal Valgus		
<b>Principal Investigator:</b> MAJ Gina J. Kim-Ahn, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Rush A. Youngberg		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Dec 99	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** Review the literature regarding radiographic determination of talocalcaneal valgus and assess the three standard radiographic measurements of talocalcaneal alignment from the Cobey view. Introduce the Cobey view to the radiology community. Correlate the clinical outcome of patients undergoing calcaneal osteotomy for talocalcaneal valgus with each of the three measurements.

**Technical Approach:** Review of charts of patients who have had the Cobey view will be performed. For each patient's Cobey view, three measurements for the talocalcaneal valgus will be made independently by two radiologists. These measurements will be compared to each other and correlated with clinical assessment and selection for surgery. The readers will be blinded to patients' subsequent clinical management. Both initial and follow-up Cobey views will be assessed. Charts of post-operative patients will also be reviewed to assess outcome.

**Progress:** 64 patients were analyzed in this retrospective study. Radiographic measurements of calcaneovalgus deformity correlated well with clinical presentation. Of the four techniques studied, the Kim-Ahn measurement was the most obtainable and it provided a high predictive value for surgical interventions.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/093	<b>Status:</b> Ongoing
<b>Title:</b> Magnetic Resonance Imaging of the Sternum		
<b>Principal Investigator:</b> CPT Andrea R. Manzo, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Rush A. Youngberg; LTC John D. Pitcher Jr., MC		
<b>Start Date:</b> 7/17/1998	<b>Est. Completion Date:</b> May 99	<b>Periodic Review:</b> 8/24/1999

**Study Objective:** To determine the magnetic resonance imaging characteristics of the normal sternum and anatomical variations.

**Technical Approach:** We propose to study 25 adults with no prior history of trauma using a torso array coil. MR images will be obtained in T1-weighted sequences in the sagittal and coronal planes. The patients we propose to study will be patients scheduled for MR imaging for other indications.

**Progress:** 5 subjects were enrolled in this study in FY00, for a total of 17 subjects enrolled at MAMC. MRI sequences have been perfected and respiratory motion compensated for. Adequate progress has been made to establish appearance of normal versus variant anatomy.

### Detail Summary Sheet

Date: 29 Sep 00                      Number: 98/106                      Status: Terminated

Title: Peri-Hepatic Lymphadenopathy in Patients with Chronic Hepatitis

Principal Investigator: MAJ Sean P. Murray, MC

Department: Radiology

Facility: MAMC

Associate Investigator(s): MAJ Daniel W. Walsh, MC; COL Amy M. Tsuchida, MC

Start Date:  
9/15/1998

Est. Completion Date:  
Sep 99

Periodic Review:  
9/15/1998

**Study Objective:** Retrospective study evaluating abdominal computed tomography (CT) for abdominal lymphadenopathy in patients with either laboratory or histologic evidence of chronic hepatitis. Correlation will be made between radiology results and subtypes of hepatitis.

**Technical Approach:** Patients with histologic or laboratory evidence of hepatitis over the past four years will be identified through a computer search. The radiologic records of these patients will then be examined. Patients with both hepatitis and an abdominal CT scan within one year will be included in the study. Patients with known malignancy will be excluded. The abdominal CT scan will be evaluated for the presence of enlarged peri-hepatic lymphadenopathy. The incidence, location and size of the lymphadenopathy will be correlated to hepatitis subtypes.

**Progress:** This study has been terminated due to the ETS of its original PI.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/069	<b>Status:</b> Completed
<b>Title:</b> Percutaneous Image-Guided Biopsy Service: Improved Diagnostic Yield with Case-Specific Use of Computed-Tomography, Ultrasound, and Fluoroscopy		
<b>Principal Investigator:</b> MAJ Sean P. Murray, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Michael C. Royer, MC; CPT Paul J. Cunningham, MC; Troy H. Patience, B.S.		
<b>Start Date:</b> 5/25/1999	<b>Est. Completion Date:</b> May 00	<b>Periodic Review:</b> 5/23/2000

**Study Objective:** To determine success of comprehensive percutaneous biopsy service, with biopsy-imaging method designed to maximize tissue sampling and diagnostic accuracy.

**Technical Approach:** Percutaneous image-guided fine-needle aspiration of masses has become a common method of diagnosis of malignancy. The choice of image modality best suited for guiding the biopsy is not clear. Whether CT, US, or fluoroscopy is used traditionally depends on personal preference and experience of the radiologist. Each imaging method may have particular advantages or disadvantages related to specific masses or patients. The consolidation of image-guide biopsies within a single service and its resultant effect on efficacy and safety has not been previously evaluated. The purpose of this retrospective study is to determine the safety and efficacy of a comprehensive percutaneous biopsy service, with biopsy-imaging method designed to maximize tissue sampling and diagnostic accuracy.

**Progress:** Work on this study has been completed; however, due to the ETS of the PI, an abstract was not available at the time of this report.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 98/034      **Status:** Ongoing

**Title:** Computed Tomography Guided Percutaneous Placement of Injection Coils Ligated to Suture and Thoracoscopic Pulmonary Resection

**Principal Investigator:** CPT John P. Reinschmidt, MC

**Department:** Radiology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Lawrence M. Casha, MC; MAJ Sean P. Murray, MC; MAJ David P. Tracy, MC; James H. Timmons, MD; MAJ Scott C. Williams, MC; LTC Maceo Braxton Jr, MC

**Start Date:**  
12/18/1997

**Est. Completion Date:**  
Indef

**Periodic Review:**  
4/25/2000

**Study Objective:** The primary objective is to reduce the number of displaced localization devices by the use of a Cook helical coil tied to a suture line as an alternative to the hookwire for VATS. A secondary objective is to reduce damage that occurs with displacement of wires.

**Technical Approach:** Twenty patients already slotted for needle localization with Hawkins III wires will have either coils attached to suture or hookwires placed. They will then be taken to the OR and thoracic surgery will remove the coils or hookwires with VATS. The degree of displacement and associated complications will be compared to our current 90% Hawkins III wire displacement rate.

**Progress:** 3 subjects were enrolled in FY00, for a total of 16 subjects (9 microcoil, 7 hookwire) at MAMC. This protocol continues to enroll subjects with an ultimate enrollment goal of 20. There have been no adverse events associated with this study.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/099	<b>Status:</b> Ongoing
<b>Title:</b> Comparison of MRI with Bone Scintigraphy in the Evaluation of Suspected Hip Stress Fractures			
<b>Principal Investigator:</b> CPT Paula J. Shepherd, MC			
<b>Department:</b> Radiology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Jerome Billingsley, M.D.; Rush A. Youngberg			
<b>Start Date:</b> 9/28/1999	<b>Est. Completion Date:</b> Dec 99		<b>Periodic Review:</b> 9/26/2000

**Study Objective:** To determine whether MRI is at least as sensitive, and possibly more specific than bone scintigraphy in the detection of hip stress (fatigue) fractures.

**Technical Approach:** The first 50 consecutive patients who present for an initial bone scan or MRI to evaluate for hip stress (fatigue) fracture as ordered by their health care providers, will be consented for both studies (bone scan and MRI) if they agree to participate in the study and meet the URI screening criteria. Results are available to clinicians upon completion of the interpretation of each study. Patients will undergo the alternate study within 5 days of completion of the study for which the patient initially presented. Plain films are not required prior to either study, however are often already obtained before presenting for further imaging. If obtained, these films are available for review by both the nuclear medicine physicians and MRI radiologists interpreting the studies; however the diagnosticians are blinded to the results of the alternate study (bone scan or MRI). The appropriate statistical test is the McNemar test, as the subjects are paired. There is no gold standard for diagnosing hip stress fractures.

**Progress:** No work was initiated on this study during FY00.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 200/089	Status: Completed
Title: Retrospective Comparison of Indirect Shoulder MR Arthograms with Arthroscopy		
Principal Investigator: CPT Scott C. Wright, MC		
Department: Radiology	Facility: MAMC	
Associate Investigator(s): Rush A. Youngberg		
Start Date: 6/27/2000	Est. Completion Date: May 00	Periodic Review: N/A

**Study Objective:** To demonstrate the accuracy of indirect MR arthograms of the shoulder in detecting pathology leading to shoulder instability.

**Technical Approach:** Retrospective chart review of MAMC patients referred for magnetic resonance (MR) imaging of the shoulder over the past three years who have history and physical examinations suspicious for instability and have undergone indirect magnetic resonance arthograms (IMRA). Arthroscopic reports will be obtained from medical records and retrospectively compared with IMRA findings.

**Progress:** Records of 15 patients identified as having had both IMRA and surgical arthroscopy were reviewed. IMRA had a sensitivity of .92, specificity of .73, and overall accuracy of .93 for Bankart lesions, and a sensitivity of .50, specificity of .73, and overall accuracy of .66 for SLAP lesions. In all patients IMRA detected either a Bankart lesion or SLAP or both. All patients had a positive arthroscopy for either or both lesions. Therefore, when IMRA detected one or both lesions (composite index) the sensitivity and specificity for anatomic abnormality accounting for the patients' symptoms were 1.00 and 1.00, respectively. Conclusion: Indirect MR arthrography provides an accurate, cost-effective and logistically better alternative to direct MR arthrography. Indirect MR arthrography should be strongly considered in patients referred with clinical findings of shoulder instability.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/166

**Status:** Ongoing

**Title:** Cost Effectiveness of Early MRI in Traumatic Wrist Injury

**Principal Investigator:** Rush A. Youngberg

**Department:** Radiology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Richard S. Makuch, MC; COL John M. Bauman, MC; CPT John D. Crocker, MC; S. P. Scheer, M.D.

**Start Date:**  
8/18/1995

**Est. Completion Date:**  
Feb 96

**Periodic Review:**  
8/20/1998

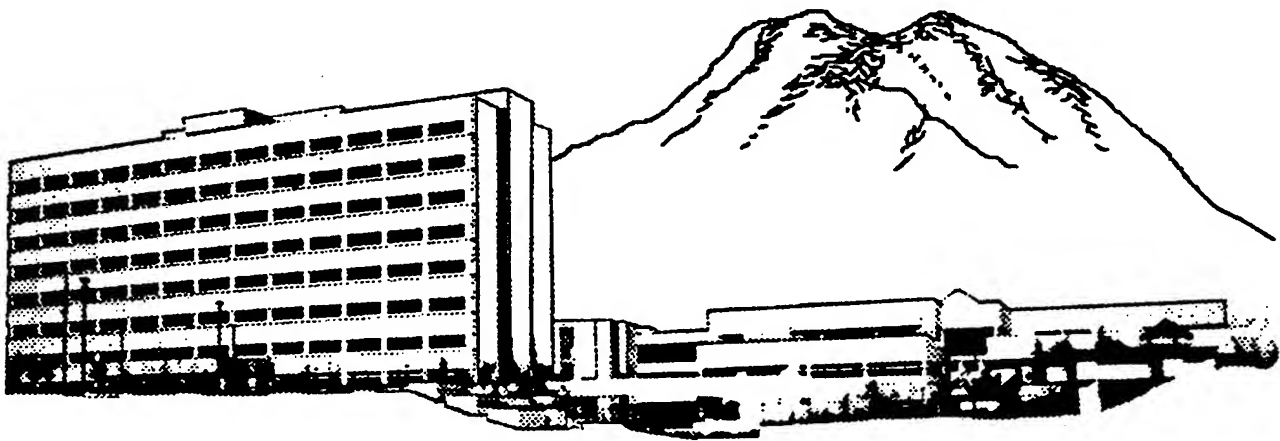
**Study Objective:** To determine the cost effectiveness and utility of scintigraphy in the management of patients with traumatic wrist injury whose initial radiographs are negative, yet who clinically are felt to have scaphoid fractures.

**Technical Approach:** This is a prospective blinded study to determine the cost effectiveness of a more accurate, slightly more expensive imaging modality in the management of patients with traumatic wrist injury. All patients over 18 years of age with a fall on the outstretched hand (a "FOOSH" injury) will be included. One hundred patients will be enrolled

Those enrolled in the study will undergo a limited high resolution bone scan of each wrist (the uninjured wrist will serve as a comparison to the injured wrist) within 48-96 hours of the time of injury. When the clinician has determined that management is complete, the clinician will have access to the bone scan results, prior to the patients' discharge from care

The radiographs will be reviewed by the chief of musculoskeletal radiology, the bone scans by a staff nuclear medicine physician, and the clinical evaluation and follow-up will be performed per usual orthopedic clinic practice at MAMC. Costs will be calculated based on the CHAMPUS allowable reimbursement for the services rendered as defined by the 1995 CPT codes of the American Medical Association. Data analysis will include determining if there is statistical significance between the costs of caring for clinically "false positive" fractures and the costs of early bone scintigraphy.

**Progress:** 2 subjects were enrolled into this protocol in FY00 for a total enrollment of 33 subjects. No conclusions have been drawn at this time. Enrollment is ongoing at MAMC.



## Detail Summary Sheets

Ft. Lewis Ranger Battalion

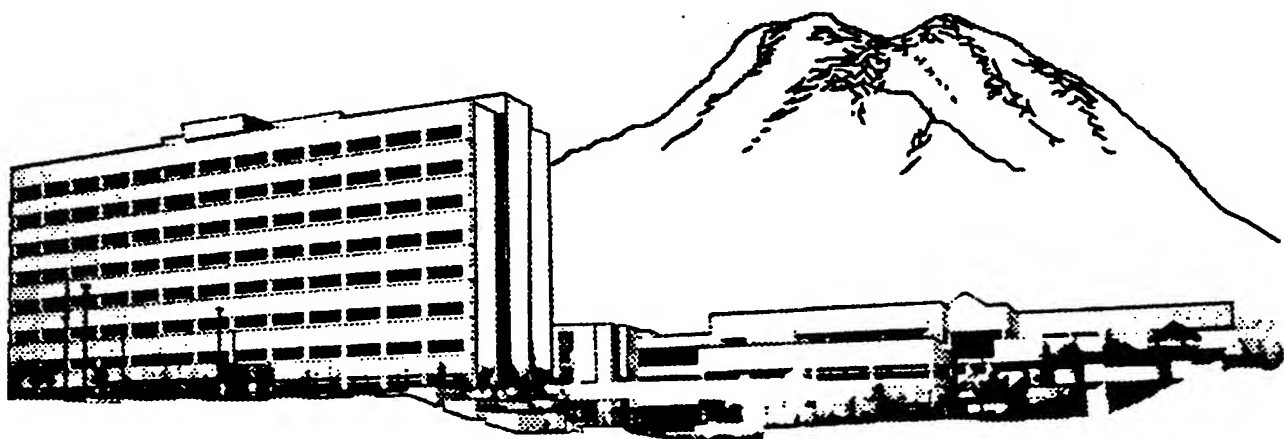
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 97/117	<b>Status:</b> Terminated
<b>Title:</b> Special Operations Medical NCO Sustainment Training Using the Goat Model (Capra hircus)			
<b>Principal Investigator:</b> CPT Charles Taylor, MC			
<b>Department:</b> Ft. Lewis Rangers Battalion		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> 2LT David Nieman, PA-C, MS-SP; SFC Paul Linskens			
<b>Start Date:</b> 7/18/1997	<b>Est. Completion Date:</b> Jul 00		<b>Periodic Review:</b> 9/30/1998

**Study Objective:** Ranger medical personnel will be exposed, gain experience and demonstrate proficiency in the following invasive resuscitation procedures: cricothyroidotomy (needle and surgical), endotracheal intubation, needle thoracentesis, chest tube placement, pericardiocentesis, intravenous catheterization, venous cutdown and techniques of suture placement.

**Technical Approach:** Anesthetized adult goats will be used to train Ranger medical personnel basic surgical and emergency resuscitation skills they are expected to perform in combat. These tasks are identified by the American College of Surgeons in the Advanced Trauma Life Saving course. Ranger medical personnel must achieve a score of 70% on the written exam at the conclusion of the didactic instruction before proceeding to the hands on portions of the exercise. This protocol does not vary from previously accepted regimens for this purpose.

**Progress:** One session was reported, Aug 97. No further sessions have been held as the protocol has been suspended pending assignment of a new PI by the Special Operations Unit. This animal use protocol reached its triennial reapproval date, 18 Jul 00, and has been terminated at MAMC.



## Detail Summary Sheets

Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/008	<b>Status:</b> Terminated
<b>Title:</b> A Randomized, Prospective, Multi-site, Open Label, Comparative 12 Week Study to Evaluate Wound Healing, Select Performance Characteristics and Cost Effectiveness of Mepilex Safetac TECHNOLOGY Wound Dressing Versus DuoDerm CGF for the Management of 60 Evaluable Patients with Venous Ulcers		
<b>Principal Investigator:</b> COL Charles A. Andersen, MC		
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Vickie R. Driver, MS, DPM; LTC Stephen B. Olsen, MC		
<b>Start Date:</b> 10/26/1999	<b>Est. Completion Date:</b> Mar 00	<b>Periodic Review:</b> N/A

**Study Objective:** To compare the treatment of Mepilex and DuoDerm CGF when treating venous leg ulcers, in terms of proportion of patients in each group that are healed (dates to healing) no later than after 12 weeks of treatment.

**Technical Approach:** This is a randomized, prospective, multi-site, comparative 12-week-study to evaluate wound healing, select performance characteristics and cost effectiveness of Mepilex safetac TECHNOLOGY wound dressing versus DuoDerm CGF for the management of patients with venous ulcers. Sufficient patients will be screened to enroll up to 60 evaluable patients in this study. During the treatment period, the condition of the study ulcer will be evaluated on a weekly basis. Outcome variables include: wound etiology, location, duration, status, dimensions, wound depth, condition of wound base, condition of the sound edges, condition of the periwound skin, exudate type and level, odor, ulcer pain, dates to healing, quality of life parameters, wound management cost effectiveness, number of skilled nursing visits, and digital wound photography and tracing. The study data will be presented as raw data listings, grouped according to the primary and secondary study objectives. Appropriate descriptive statistics will be computed and presented on an 'intent to treat' basis. All adverse events and adverse device events will be reported. There will be no hypothesis testing at baseline.

**Progress:** This protocol was closed to patient entry ,19 Apr 00, per study sponsor due to an inability to recruit sufficient subjects and inconsistencies in data obtained to date. Four subjects enrolled at MAMC. One subject was withdrawn from study participation due to an adverse event which was considered unrelated to study participation. Three subjects completed follow-up, and the study was reported as terminated, 16 Aug 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/088	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Randomized Study Comparing the Outcome of Carotid Endarterectomy Using New Generation Dacron or Expanded Polytetrafluoroethylene (e-PTFE) Carotid Patching		
<b>Principal Investigator:</b> COL Charles A. Andersen, MC		
<b>Department:</b> Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Stephen B. Olsen, MC; COL David F. J. Tollefson, MC		
<b>Start Date:</b> 5/23/2000	<b>Est. Completion Date:</b> Jun 02	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to compare the performance of the newest generation Dacron and e-PTFE patches with respect to: (1) postoperative stroke/thrombosis, (2) recurrent carotid stenosis and (3) intraoperative handling/blood loss.

**Technical Approach:** After informed consent, patients will be randomized to patch angioplasty with either a Hemashield Finesse patch or a Gore-Tex Acuseal patch. Surgeons will rank the handling of the patch on an analog scale. Time to cessation of bleeding will be monitored. Patients will have an intraoperative duplex , and follow-up duplex examinations at 3, 6, 9, 12, 18 and 24 months after the operation. Rates for carotid restenosis will be determined. Perioperative and late neurologic morbidity will be identified and determined.

**Progress:** No patients have been enrolled in this study in FY00 at MAMC.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 96/163

**Status:** Ongoing

**Title:** Clinical Evaluation of the Handling and Performance of the HEMASHIELD Knitted Double Velour Fabric and Polytetrafluoroethylene (PTFE) Patched for Carotid Endarterectomy Patch Procedures in Patients

**Principal Investigator:** COL Charles A. Andersen, MC

**Department:** Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; Edmund A. Kanar; George J. Collins, Jr.

**Start Date:**  
9/20/1996

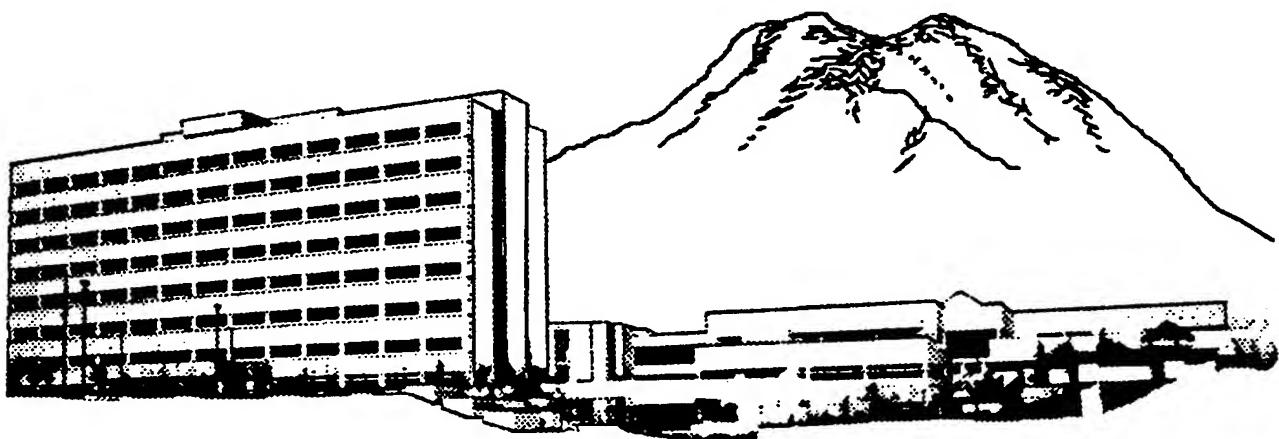
**Est. Completion Date:**  
Nov 98

**Periodic Review:**  
9/26/2000

**Study Objective:** The objective of this randomized, parallel group, multi-center study is to evaluate the performance of the test product, the HEMASHIELD® Knitted Double Velour patch in comparison to the control product, the Gore-Tex patch, for use as a carotid artery patch following carotid endarterectomy in patients.

**Technical Approach:** This is a prospectively randomized, multi-center clinical trial in which a maximum of 40 patients will be enrolled, with approximately equal numbers of patients in each of the 2 treatment groups, Hemashield patch vs. the Gore-Tex patch. Anticipated MAMC enrollment is approximately 20 patients. Patients included in this study will be evaluated preoperatively, intraoperatively, at discharge from the hospital, and at 3 months, 6 months, 12 months and up to a total of 24 months postoperatively. Follow-up evaluations will include a medical history and physical exam at 3, 6, 12 and 24 months and duplex ultrasound testing at 6 and 12 months (with optional duplex scan at 24 months) for assessment of patch repair. Completion of follow-up assessment and final report is anticipated about one and one half years after the first patient enrollment.

**Progress:** One patient was entered into this protocol FY00, for a total of 40 patients enrolled. This study is closed to patient enrollment; however patient follow-up will continue through Nov 2001. No adverse events have been reported.



## Detail Summary Sheets

General Surgery Service,  
Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/098	<b>Status:</b> Terminated
<b>Title:</b> Gastrin Releasing Peptide Receptor: A Potential Novel Marker of Clinical Aggression in Human Neuroblastoma Cells		
<b>Principal Investigator:</b> CPT Alec C. Beekley, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Ann O'Connor, M.D.; Robert S. Sawin, M.D.; CPT James A. Sebesta, MC; Katherine H. Moore, Ph.D.; LTC Kenneth S. Azarow, MC		
<b>Start Date:</b> 8/20/1998	<b>Est. Completion Date:</b> Jul 99	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** To determine whether the expression of Gastrin Releasing Peptide Receptor by human Neuroblastoma cells correlates with increased malignancy.

**Technical Approach:** By using the fluorescent peptide technology described below, this study proposes to demonstrate that: 1) gastrin releasing peptide receptor is expressed by human neuroblastoma cells, and 2) expression of this receptor may correlate with advanced malignancy. The established cell lines will be grown to confluence at MAMC. After appropriate washes, cells will be incubated with Fluo-GRP which is expected to bind specifically to the GRP receptor on those cells which express it. Following incubation, cells will be fixed and studied under fluorescence microscopy to visualize cell surface binding and internalization of the labeled receptor. Future investigation will focus on analysis of fresh frozen sections of tumors from patients with neuroblastoma in the hopes that GRP receptor expression can be used both as a marker of advance disease, and as a potential target for specific anti-GRP receptor therapy.

**Progress:** Kits required to perform work on this study were not forwarded from Children's Hospital, Seattle, WA, during FY00; therefore, the PI has chosen to terminate this project.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/005	<b>Status:</b> Ongoing
<b>Title:</b> Surgical Skills Practicum - Advanced Trauma Life Support for Doctors (ATLS) Using the Goat ( <i>Capra hircus</i> )		
<b>Principal Investigator:</b> COL William E. Eggebroten, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Kenneth S. Azarow, MC		
<b>Start Date:</b> 10/20/1998	<b>Est. Completion Date:</b> Oct 01	<b>Periodic Review:</b> 10/10/1999

**Study Objective:** The objective of this training exercise is to teach physicians one safe method of performing six lifesaving procedures for trauma patients.

**Technical Approach:** This training protocol will instruct MAMC residents in the initial management of trauma patients. The students will practice the safe methods of performing the following lifesaving procedures in the order listed: venous cutdown, peritoneal lavage, chest tube placement, pericardiocentesis, thoracotomy and vessel cross clamp, cricothyroidotomy. The procedures will be performed after the animals are properly prepared and adequately anesthetized for surgery. The endpoint of this training will be completion of all procedures or evidence of excessive duress or anesthetic instability. Students will be evaluated by instructors on the basis of direct observation of psychomotor skills and verbalization of the indications, contraindications and potential complications of each procedure.

**Progress:** Four training sessions were held in FY00, which used 12 goats and 4 pigs total. Evaluations by instructors stated that training taught under this protocol proved very helpful to interns and junior residents. This training protocol remains ongoing at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/083

**Status:** Ongoing

**Title:** Porcine Iliac Artery Injury Model for Testing of Absorbable Vascular Templates

**Principal Investigator:** CPT Mohamad I. Haque, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Scott R. Steele, MC; LTC Kenneth S. Azarow, MC; COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC; COL William C. Williard, III, MC; MAJ David P. Tracy, MC; MAJ Sean P. Murray, MC; COL Charles A. Andersen, MC; CPT Alec C. Beekley, MC; MAJ Ronald E. Nielsen, VC

**Start Date:**  
6/19/1998

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
8/24/1999

**Study Objective:** (1) To determine if pigs can serve as an adequate living tissue model for testing the in vivo absorption of polyphosphasene vascular templates and (2) if the absorbable vascular templates or stents will effectively treat deliberate, non-transecting iliac artery injuries in a porcine model in a reproducible fashion.

**Technical Approach:** An absorbable template will be unilaterally placed in each pig's normal iliac artery using manual and angiographic techniques via an arteriotomy in the opposite iliac artery. Impact of the stent will be assessed immediately through intraoperative arteriographic measurement of luminal diameters. Impact of the templates over time will be assessed by repeat angiography with subsequent sacrificing of the animals and tensile strength testing, routine histopathologic evaluation, and electron microscopic evaluation of the arterial segment containing the experimental stent at one, two, three, four, and five weeks after stent placement

Bilateral, non-transecting iliac arteriotomies will be created in a standard fashion in each pig, placing an experimental absorbable vascular template across one lesion using manual, endovascular and/or angiographic techniques, and primarily repairing the opposite lesion with standard vascular suture techniques. Resulting artery and stent patency and integrity will be assessed by intraoperative arteriography. Impact over time will be assessed via repeat arteriography with subsequent sacrifice of the animals and tensile strength testing, routine histopathologic evaluation, and electron microscopic evaluation of the segments of artery containing the experimental stent at one, two, three, four, and five weeks following stent implantation. These results will be compared with the results of the same tests done on the arteriotomies that were repaired primarily with suture.

**Progress:** This protocol remains ongoing while awaiting the production of the vascular stents. No work was accomplished on this protocol in FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/133	<b>Status:</b> Ongoing
<b>Title:</b> Development of an In-vivo Model of Free Radical Production Utilizing Dihydroethidine in the Rat ( <i>Rattus Norvegicus</i> )		
<b>Principal Investigator:</b> CPT Rebecca E. Marier, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Jerome M. McDonald, MC; CPT Todd M. Rossignol, MS; LTC Kenneth S. Azarow, MC		
<b>Start Date:</b> 9/13/2000	<b>Est. Completion Date:</b> Sep 03	<b>Periodic Review:</b> N/A

**Study Objective:** To determine a reproducible and inexpensive method of quantitatively measuring free radical production in the rat.

**Technical Approach:** This study will utilize 10 "control" rats and 10 "test" rats that have been anesthetized and then subjected to ischemia/reperfusion by clamping and then unclamping the aorta above the celiac trunk. A fluorescent label for the presence of free radicals (specifically superoxide) will be injected during the experiment. The animals will be sacrificed and specified organs analyzed using a spectrophotometer for quantitation of the production of superoxide. In addition, a well-known marker of lipid peroxidation, malondialdehyde (MDA) will be measured to verify that the free radical superoxide has indeed been produced.

**Progress:** This study takes the place of protocol #99021. Work is scheduled to begin on this project October 2000.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/021	<b>Status:</b> Terminated
<b>Title:</b> Development of an In-vivo Model of Free Radical Production Utilizing Dihydroethidine in the Rat (Rattus norvegicus)		
<b>Principal Investigator:</b> CPT Rebecca E. Marier, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David C. Elliott, MC; Katherine H. Moore, Ph.D.; LTC Kenneth S. Azarow, MC; CPT Jerome M. McDonald, MC		
<b>Start Date:</b> 1/26/1999	<b>Est. Completion Date:</b> Jan 02	<b>Periodic Review:</b> N/A

**Study Objective:** To generate an inexpensive and accurate model of in-vivo free radical production and quantification utilizing mice.

**Technical Approach:** Anesthetized animals will undergo a mid line laparotomy and the supra celiac aorta will be cross clamped for 30 minutes to generate ischemia. At 10 minutes post-clamping, 20umoles per liter estimated total body water of hydroethidine will be injected into the right iliac vein. At time 30 minutes, the clamp would be removed slowly and reperfusion for 15 minutes would commence. Following reperfusion, the aorta would be transected at the diaphragm and using a 14 gauge angiocatheter, would be flushed with normal saline to wash out residual hydroethidine and ethidium bromide. The liver, pancreas, small bowel, stomach and lungs would be rapidly removed and frozen in liquid isopentane utilizing OCT freezing medium. The specimen would then be sectioned on a cryostat at 12 um, placed on a slide, and evaluated under a standard rhodamine filter fluorescent microscope.

Photo documentation or fluorescence quantitation will then be performed. Ethidium bromide staining of the tissue after quantitation would allow for standardization of tissues in regard to total number of nuclei. Utilizing different time points in this model to maximize reactive oxygen species identification will be necessary. Utilization of nitrogen gas to minimize background may be necessary in preparation of the hydroethidine and in several steps of tissue processing.

**Progress:** This protocol was terminated due to the PCS of its principal investigator prior to final IACUC approval. The new principal investigator chose to rewrite the protocol and submit as a separate study.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/074

**Status:** Ongoing

**Title:** Introduction of Telomerase into Type II Pneumocytes: Effect on Life span and Surfactant Production

**Principal Investigator:** CPT Matthew J. Martin, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Scott R. Steele, MC; CPT Todd M. Rossignol, MS; LTC Kenneth S. Azarow, MC

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Nov 00

**Periodic Review:**  
N/A

**Study Objective:** (1) Determine whether cells purchased from ACT will not have any significant telomerase activity or surfactant production prior to transfection with hTERT, (2) If ACT cells exhibit telomerase activity then they will not be used and we will attempt to culture and sustain a population of normal rat type II pneumocytes, (3) Transfect normal rat type II pneumocytes with a vector including the human telomerase catalytic subunit, (4) Assess telomerase activity in transfected cell population and control group, (5) Assess telomere length in transfected cell population and control group, (6) Assess pulmonary surfactant production in transfected cell population and control group, and (7) Stain transfected cell population and control group for B-galactosidase, a biological marker for cellular aging.

**Technical Approach:** Type II pneumocytes (CCL-149) will be purchased from ACT and grown to confluence. The cells will be extracted and telomerase activity will be assayed. If the cells exhibit a negative telomerase activity, then they will be used for the remainder of the study, if not, then a population of normal rat type II pneumocytes will be cultured from a rat lung. The appropriate cells will then be transfected with the nTERT cDNA gene. This will be accomplished using one of the procedures of transfection, either the bombardment techniques, Lipofectin or other. After transfection and growth of the cells to confluence, the cells will be assays again for Telomerase activity as above. Non transfected cells will be used as a control group. Telomere length will be determined. Pulmonary Surfactant production will be measured using either Western Analysis or another method as well as B-Galactosidase activity as a biological marker of cell aging.

**Progress:** This protocol is currently waiting for contract approval and delivery of materials. Pneumocyte cell cultures have been started.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/078

**Status:** Ongoing

**Title:** Inflammatory Response Related to Tracheobronchial Distention in Pigs (*Sus scrofa*) Using Absorbable Tracheal Stents

**Principal Investigator:** CPT Matthew J. Martin, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Ronald A. Gagliano, MC; CPT Alec C. Beekley, MC; CPT Leroy J. Trombetta, MC; MAJ Andrew B. Silva; LTC Kenneth S. Azarow, MC

**Start Date:**  
5/22/1998

**Est. Completion Date:**  
May 01

**Periodic Review:**  
9/13/2000

**Study Objective:** To characterize the inflammatory reaction and granulation tissue formation following absorbable stent placement in the pig airway. To achieve this long term objective, our pilot should demonstrate any differences between in vivo and in vitro absorption of the stents.

**Technical Approach:** A total of 10 pigs will be utilized in this study, two pigs per group during a 5 week period of time. Group 1 will have stent insertion with sacrifice of the animals at day 7; Group 2 will be sacrificed at day 14; Group 3 will be sacrificed at day 21; Group 4 will be sacrificed at day 28 and Group 5 will be sacrificed at day 35. All animals will undergo histologic examination of their airways to include videoscopic recordings in order to more accurately measure airway lumen diameters and tissue condition and reactivity.

**Progress:** This protocol remains ongoing while awaiting the production of a tracheal stent. No work was accomplished on this protocol in FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/142

**Status:** Ongoing

**Title:** A Prospective, Randomized, Double-blind, Multicenter Trial Assessing the Safety and Efficacy of Sequential (intravenous/oral) BAY 12-8039 (moxifloxacin) 400 mg every 24 hr Compared to Intravenous Piperacillin/Tazobactam 3.375 gm every 6 hr Followed by Oral Amoxicillin/Clavulanic Acid Suspension 800 mg every 12 hr for the Treatment of Patients with Complicated Intra-abdominal Infections

**Principal Investigator:** MAJ Ronald J. Place, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** None.

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Feb 02

**Periodic Review:**  
N/A

**Study Objective:** To compare the safety and efficacy of sequential (intravenous/oral) moxifloxacin every 24 hours with the combination of intravenous piperacillin/tazobactam (Zosyn\*) every 6 hr followed by oral amoxicillin/clavulanic acid (Augmentin\*) suspension every 12 hours for the treatment of adult patients with complicated intra-abdominal infections.

**Technical Approach:** The primary diagnosis of each patient in this study will be complicated intra-abdominal infection defined as an intra-abdominal infection in which an operative procedure or percutaneous drainage is required for diagnosis and management. Findings at operation must confirm the presence of an intra-abdominal infection (e.g., presence of purulent exudate and inflamed or necrotic tissue).

Patients will be randomized to one of two treatment groups. Treatment Group 1: Experimental treatment arm of Moxifloxacin 400 mg, administered by intravenous infusion over 60-minutes every 24 hours plus a piperacillin/tazobactam placebo infusion every 6 hours. If the patient is switched from intravenous to oral moxifloxacin 400 mg tablet every 24 hours, they will also receive amoxicillin/clavulanic acid placebo suspension every 12 hours.

Treatment Group 2: Standard treatment arm of Piperacillin/Tazobactam 3.375 gm, administered by intravenous infusion over 60-minutes every 6 hours plus a moxifloxacin placebo infusion every 24 hours. If the patient is switched from intravenous piperacillin/tazobactam to oral amoxicillin/clavulanic acid suspension 800 mg every 12 hours, they will also receive a moxifloxacin placebo tablet every 24 hours.

For both treatment groups, at the investigator's discretion, a switch to oral therapy could be made if the following criteria are met; (1) patient is clinically improving on intravenous therapy, (2) gastrointestinal motor activity has returned as indicated by passage of gas or feces per rectum or ostomy or (3) gastrointestinal function is present as indicated by tolerance of enteral feedings, either by mouth or by tube (including jejunostomy). Patients will be evaluated for complete recovery.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/004	<b>Status:</b> Ongoing
<b>Title:</b> Forward Surgical Team (FST) Sustainment Training Using the Goat Model ( <i>Capra hircus</i> )		
<b>Principal Investigator:</b> LTC Clifford A. Porter, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David C. Elliott, MC; MAJ Ann Everett, AN, CRNA; CPT Michael S. Murphy, AN; LTC Craig M. Ono, MC		
<b>Start Date:</b> 10/20/1998	<b>Est. Completion Date:</b> Oct 01	<b>Periodic Review:</b> 8/11/2000

**Study Objective:** FST personnel will be exposed, gain experience and demonstrate proficiency in invasive resuscitation procedures.

**Technical Approach:** FST personnel must achieve a score of 70% on the written exam at the end of the didactic instruction before proceeding to the hands on portion of the exercise. Anesthetized adult goats will be used to train medical personnel basic surgical and emergency resuscitation skills they are expected to perform in combat. These tasks include: cricothyroidotomy (needle and surgical), endotracheal intubation, needle thoracentesis, chest tube placement, open thoracotomy, peritoneal lavage, exploratory laparotomies (FST surgeons), pericardiocentesis, intravenous catheterization, venous cutdown and techniques of suture placement (abdominal fascial closure). This protocol doesn't vary from previously accepted regimens for this purpose.

**Progress:** No progress was made on this protocol during FY00, due to prolonged deployment of the team to Macedonia/Kosovo.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/087

**Status:** Ongoing

**Title:** Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig (Sus scrofa)

**Principal Investigator:** LTC Clifford A. Porter, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL William E. Eggebrotten, MC; COL William C. Williard, III, MC; LTC Kenneth S. Azarow, MC; LTC Alan L. Beitler, MC; LTC David C. Elliott, MC; LTC David M. Watts, MC; Preston L. Carter, M.D.

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Aug 02

**Periodic Review:**  
10/11/2000

**Study Objective:** To familiarize General Surgery residents, staff and invited surgeons from our community with techniques in the performance of advanced laparoscopic techniques. This training will include esophagus, stomach, biliary, small and large intestine, spleen, liver and retroperitoneal procedures. The training benefit will accrue to General Surgery residents, staff and invited surgeons by introducing these techniques or reinforcing earlier acquired skills in a controlled environment. Familiarity with these techniques will allow an increased margin of safety for patients decreased operative time, and minimizing of potential complications.

**Technical Approach:** Pigs will be maintained in an NPO status for 12 hours prior to the scheduled training procedures. An intramuscular tranquilizer will be used to aid in animal handling and preoperative management. General anesthesia will be induced with injectable agent and maintained by inhalational agent. Following anesthesia induction, pigs will be intubated endotracheally, will have an indwelling intravenous catheter placed in an ear vein for intraoperative fluid support, will have an orogastric tube inserted and connected to central suction for as-needed gastric decompression, and will be clipped and scrubbed as per aseptic surgery technique for the body regions of interest (e.g. abdomen, chest, etc.). Preoperative preparations will be conducted in the DCI animal surgery preparation and recovery room immediately adjacent to the DCI surgery. Following preoperative preparation, anesthetized animals will be transferred to either DCI surgery suite.

Five training sessions are scheduled for this training, they are: Advanced Laparoscopic Esophageal and Gastric Surgery, Advanced Laparoscopic Biliary Surgery, Advanced Laparoscopic Small and Large Intestinal and Rectal Surgery, Advanced Laparoscopic Splenectomy and Liver Surgery, and Advanced Laparoscopic Retroperitoneal Dissection and Lymph Node Dissection. Each session will be formalized into one day continuing medical education programs consisting of 1 hour of didactic lecture, 4 hours of hands-on procedural and/or instrumentation orientation using inanimate training models and non-living human or animal tissues, and 3 hours of live (anesthetized) animal laboratory for definitive procedural training. Each animal will be used for a single training session only, and will be euthanized at the end of the session without recovery from general anesthesia. Non-survival/training surgical procedures will be performed using clean (simulated aseptic) technique. Each training session will utilize up to four pigs.

**Progress:** Two training sessions were held in FY00, utilizing a total of 5 animals. Both staff and residents participated with excellent skills learned. These sessions have significantly improved medical readiness and direct patient care through enhanced skills learned.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/115	<b>Status:</b> Ongoing
<b>Title:</b> Relationship Among Differentiation, Apoptosis, and Telomerase Activity in Neuroblastoma Cell Lines		
<b>Principal Investigator:</b> CPT Christopher K. Sanborn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Kenneth S. Azarow, MC; CPT Craig S. See, MC; Robert S. Sawin, M.D.		
<b>Start Date:</b> 8/22/2000	<b>Est. Completion Date:</b> Nov 00	<b>Periodic Review:</b> N/A

**Study Objective:** Determine the level of telomerase activity in human neuroblastoma cell lines via PCR-ELISA assays before and after induced differentiation by retinoic acid. Relate telomerase activity to apoptosis using the CDDE+ technique before and after differentiation for assay.

**Technical Approach:** This study will synchronize the SK-N-DZ neuroblastoma cell line in culture by utilizing the isopyknic centrifugation technique. Baseline TRAP, CDDEplus, and pp60c-src assays on the SK-N-DZ cells will be performed to establish baseline values of telomerase activity, apoptotic activity and level of c-src expression respectively. Subculture of the cells will then be subjected to either normal culture medium or culture medium enhanced with retinoic acid. After 3, 6, and 10 days of treatment, the above assays will be performed again to analyze differences between each cell group as compared to its untreated control group.

**Progress:** This protocol did not collect enough data during FY00 to attempt data analysis at the time of this report.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/022

**Status:** Terminated

**Title:** The Use of Autologous Fibrin Glue to Prevent Post-operative Seromas in Patients Undergoing modified Radical Mastectomy

**Principal Investigator:** CPT Christopher K. Sanborn, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Patrick J. Offner, MC; CPT Daniel D. Mais, MC; CPT Bret R. Hansen, MC

**Start Date:**  
11/18/1994

**Est. Completion Date:**  
Dec 96

**Periodic Review:**  
11/17/1998

**Study Objective:** To determine if the use of autologously donated fibrin glue can decrease the incidence of post-operative fluid collections in patients undergoing modified radical mastectomy.

**Technical Approach:** We plan to conduct a prospective, randomized study evaluating the effects of autologously donated fibrin glue on the flaps created during modified radical mastectomy in attempts to increase the adhesion of the flaps to the underlying tissue and prevent post-operative fluid collections. A total of 60 subjects will be recruited and randomized to a study group and a control group. All subjects will donate one unit of autologous blood pre-operatively. This blood will be used to provide the autologous fibrinogen for the study group. Surgeons will be given the fibrin preparation or saline to apply after mastectomy. The surgeons will be blinded as to whether they are applying fibrin glue or control saline. Drainage from the surgical area will be recorded by the subjects and a blinded evaluator will assess fluid accumulation at least weekly after drains are removed. Seroma fluids will be drained as necessary. Rates of seroma formation will be compared using chi-square analysis. The mean total amount of drain output and the mean length of time for the drains to be discontinued will also be analyzed using the Student's T-test or a non-parametric test should the distribution prove to be non-Gaussian.

**Progress:** This protocol has been reported as terminated without enrolling patients. A new literature search revealed that this experimental design had been done by doctors in other institutions.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/124	<b>Status:</b> Ongoing
<b>Title:</b> Clinical Pathway for Resectional Gastric Bypass for Morbid Obesity Focusing on Postoperative Diet		
<b>Principal Investigator:</b> CPT James A. Sebesta, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Craig S. See, MC; LTC David M. Watts, MC; LTC Kenneth S. Azarow, MC; Preston L. Carter, M.D.; MAJ Ronald J. Place, MC		
<b>Start Date:</b> 8/22/2000	<b>Est. Completion Date:</b> Oct 02	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if an aggressive management of the postoperative diet can safely decrease the length of stay for the morbidly obese patients who undergo resectional gastric bypass.

**Technical Approach:** Patients will be randomized into one of two groups, the standard diet or the study diet. The patient's demographic information will be collected and recorded on the clinical pathway form. Operative and postoperative data points will be collected. All patients will receive the same anesthetic and have their postoperative pain controlled with a patient controlled anesthesia device and will be given Ketorolac 30mg IV on the evening of surgery and 15mg IV every 8 hours for 72 hours. Every patient will receive the same antibiotic, DVT prophylaxis and anti-emetics including: Cefotetan 2gm IV every 12 hours for 24 hours, Heparin 5000 mg SQ twice a day, and Inapsine 1.25 mg IV every 6 hours as needed.

All patient activity will be controlled. This will consist of out-of-bed to chair at least three times a day starting on postop day number 1; ambulate within the room at least three times per day on postop day number 2; and ambulate in the halls at least three times a day on each subsequent day. A nasogastric tube will be placed intraoperatively and will be removed on the morning of postoperative day one. Anti-emetic use is authorized and will be documented.

Subjects randomized to the standard diet will receive nothing by mouth until demonstration of full intestinal activity by the passage of flatus. The patient will then be given gastric bypass clear liquids for 24 hours. If the patient has no more than one episode of nausea requiring anti-emetics and no emesis, they will be transitioned to a post-gastric bypass diet and discharged after receiving nutritional instructions and tolerating two solid meals without nausea or emesis.

Subjects randomized to the study diet will receive nothing by mouth until the morning of postop day number two. Patients will then be started on a 30cc per hour gastric bypass clear liquid diet until 2200 hours. This will be self administered and documented by the patient. If the patient has no more than one episode of nausea requiring anti-emetics and no emesis, they will be transitioned to ad lib gastric bypass clear liquid diet for postoperative day number three. When the patient has no more nausea requiring anti-emetics or emesis for 24 hours, they will receive nutritional instructions for gastric bypass soft diet and discharged.

All patients will receive a phone call daily for three days after discharge by surgeons who are blinded to the study to monitor progress and screen for complications. Postop wound evaluations will also be performed by the same surgeons.

**Progress:** This protocol recently received review and approval by the IRB. No work was initiated on this study in FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 97/143      **Status:** Completed

**Title:** A Prospective Multi-institutional Study to Determine the Sensitivity and Specificity of Telomerase in Thyroid FNAs for the Detection of Thyroid Cancer

**Principal Investigator:** CPT James A. Sebesta, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Kenneth S. Azarow, MC; COL William C. Williard, III, MC; LTC Clifford A. Porter, MC; CPT Wade K. Aldous, MS; CPT Brenda K. Bell, MC; MAJ Raymond S. Lance, MC; MAJ Janice C. Stracener, MC; LTC Mary Maniscako-Thegerge, MC; LTC Jeffrey Kavolius, MC; LTC James North, MC; LTC Russell Martin, MC; LTC Steve Hetz, MC

**Start Date:**  
9/19/1997

**Est. Completion Date:**  
Nov 98

**Periodic Review:**  
8/22/2000

**Study Objective:** Our objective is to evaluate telomerase activity in thyroid fine needle aspirations as a screening modality for the detection of thyroid cancer.

**Technical Approach:** This study is designed to evaluate the efficacy of measuring telomerase activity in fine needle aspirations of thyroid nodules as a screening tool for thyroid carcinoma. The six Army medical centers involved include MAMC, WRAMC, TAMC, DDEAMC, WBAMC and BAMC. Patients with suspicious thyroid nodules requiring fine needle aspiration (FNA) will have additional FNA samples taken at the time of surgery sent to MAMC to determine if telomerase activity is present in the specimens. Additionally, after surgical excision of the thyroid, a sample of the primary tumor will also be sent to MAMC for evaluation of telomerase activity. The results of these tests as well as patient clinical data will be analyzed to determine the sensitivity and predictive value of telomerase as a screening tool for thyroid malignancy. We estimate the total number of patients needed to complete the study to be 360 utilizing a power analysis. The total number of specimens analyzed will be approximately 1000. The data will be collected and analyzed using statistical software to evaluate surgical correlation to telomerase activity in FNAs. Major analysis being the correlation of the biopsy cytology to the telomerase activity detectability, reporting sensitivity and specificity, along with positive and negative predictive value. The study will run for approximately one year. Consent is required for additional FNA passes for all patients.

**Progress:** This study closed to patient enrollment with 24 patients enrolled in this study at MAMC. Analyses and conclusions were not available at the time of this report.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/096

**Status:** Completed

**Title:** Gastrin Releasing Peptide: A Potential Growth Factor Expressed in Human Neuroblastoma Tumors

**Principal Investigator:** CPT James A. Sebesta, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** Ann O'Connor, M.D.; Robert S. Sawin, M.D.; Jeff M. Bullock, M.S.; LTC Kenneth S. Azarow, MC; Katherine H. Moore, Ph.D.; CPT Leroy J. Trombetta, MC; CPT Amy L. Young

**Start Date:**  
8/20/1998

**Est. Completion Date:**  
Dec 98

**Periodic Review:**  
7/27/1999

**Study Objective:** To determine whether the Gastrin Releasing Peptide and Gastrin Releasing Peptide Receptor genes are expressed in human neuroblastoma tumors, and to determine whether expression of these genes is associated with more aggressive tumor histology.

**Technical Approach:** Once the sequentially numbered tumor samples are received, the total RNA will be harvested from each tumor (per standard protocols). The technique of reverse transcription polymerase chain reaction (RT-PCR) will be used to first synthesize GRP cDNA from the total RNA, and then amplify the GRP cDNA product (per standard protocols). The same technique will be used to synthesize and amplify GRP-R cDNA. Specific primers for these experiments have been obtained from the published GRP and GRP-R gene sequences, and have been used successfully in neuroblastoma cell culture models. The above result will be confirmed using Southern Blot analysis (per standard protocol) using digoxigenin labeled probes previously generated through PCR.

**Progress:** 19 tumor specimens were obtained, ranging in biologic behavior from ganglioneuroma, the benign variant of neuroblastoma, to metastatic neuroblastomas. Total RNA was extracted from human neuroblastoma cells. A reverse transcription polymerase chain reaction was then performed using specific primers. The products of the RT-PCR were then confirmed to be GRP and GRP-R cDNA by southern blot analysis. The RT-PCR products were then sequenced and these sequences were compared to the known sequences of GRP and GRP-R DNA. Results: N-19. GRP and GRP-R mRNA were present in all neuroblastoma specimens. Although no correlation with other known predictors of poor prognosis existed, transcripts of four different sizes (400, 450, 500, and 950 base pairs) were seen in the GRP-R transcripts. The sequences of the 950 base pairs sized transcript reverse transcription PCR products were identical to the known GRP-R. Conclusions: Gastrin releasing peptide and Gastrin releasing peptide receptor mRNA are present in all human neuroblastomas. Although qualitatively, it appears to lack prognostic significance, its ubiquitous nature in the tumor suggests it may be a useful target to base future treatment modalities.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/012	<b>Status:</b> Terminated
<b>Title:</b> Comparison of the Harmonic Scalpel and the Standard Technique for Right Hepatic Lobectomy in Pigs ( <i>Sus scrofa</i> )		
<b>Principal Investigator:</b> CPT James A. Sebesta, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC David C. Elliott, MC; CPT Ronald A. Gagliano, MC; A Gant		
<b>Start Date:</b> 12/15/1998	<b>Est. Completion Date:</b> Dec 01	<b>Periodic Review:</b> N/A

**Study Objective:** To compare the time and ease of the standard fracture technique of liver resection to the heretofore undescribed method of using the harmonic Scalpel. Other factors evaluated will be blood and bile loss and the ability to complete the resection.

**Technical Approach:** Four pigs will be randomized into two groups. Group one will have the standard finger fracture technique right hepatic lobectomy. Group two will have the Harmonic Scalpel right hepatic lobectomy. Data collected will include noting the time of onset of hepatic dissection to the completion of the lobectomy, all bile and blood lost during the procedures will be collected and measured and all sponges and laparotomy pads will be weighed to estimate the fluid collected in them. A closed suction drain will be placed intraoperatively in the resection bed to measure the output for 24 hours. Irrigation will be avoided if possible, but if it is used, the amount will be recorded and subtracted from the total fluids collected. The resected portion of the liver will be submitted to pathology for evaluation of the extent of injury to the surrounding tissue.

**Progress:** This protocol was unable to find adequate funding and has been terminated at MAMC. No work was initiated on this study.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/097	<b>Status:</b> Completed
<b>Title:</b> Gastrin Releasing Peptide's Effect on Telomerase Activity in Human Neuroblastoma Cell Lines		
<b>Principal Investigator:</b> CPT Scott R. Steele, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Leroy J. Trombetta, MC; LTC Kenneth S. Azarow, MC; Katherine H. Moore, Ph.D.; Robert S. Sawin, M.D.; CPT James A. Sebesta, MC		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Jan 00	<b>Periodic Review:</b> 7/25/2000

**Study Objective:** To determine the effect of Gastrin Releasing Peptide (GRP) on telomerase activity in neuroblastoma cell lines.

**Technical Approach:** Neuroblastoma (IMR32) and small cell lung carcinoma cell lines (H345) will be maintained in 5% fetal bovine serum and supplemented with 100 units of penicillin per ml, 100 ug of streptomycin per ml, 2.5 ug amphotericin B per ml at 370 C under 5% CO<sub>2</sub>. Cultures will be grown in 25 cm<sup>2</sup> flasks and seeded with approximately 3.5E5 per inoculum.

Experiment One - Determination of basal production of Gastrin Releasing Peptide (GRP) from cultured cells. Previous work has shown that these cells express GRP mRNA. In order to know how much peptide and antibody to use in the following experiments, a measurement of the basal production of GRP from the cultured cells is essential. In addition, the basal activity of telomerase will be determined. Cells will be grown in culture for three days. Control flasks will be trypsinized for total cell counts and harvested for telomerase activity. Initially, 1000 cells will be used for the telomerase assay and then adjusted to provide the greatest sensitivity of the assay. Telomerase activity will be determined using the TRAP assay according to the manufacturers directions (Roche Molecular Biochemicals). RIA for GRP will be performed according to the manufacturer's instructions (Phoenix Pharmaceuticals). GRP will be separated for the growth media and other cellular products using a size exclusion filter that retains proteins larger than 10 kDa. GRP is 2859 Da, and will flow through the filter. Larger proteins that may interfere with the RIA will be retained behind the filter. Preliminary experiments will be performed to determine parallelism of the assay for GRP produced in cell culture, and to determine recovery.

Experiment Two -The cell lines will then be grown in the presence of the monoclonal antibody for GRP, 2A11. The monoclonal antibody 2A11 has been obtained from NCI, Navy Medical Oncology Branch, Bethesda, MD. The amount 2A11 used in the culture will be based on the baseline determination of GRP production of the cell lines. Cells will be grown in culture for 8 days, with cells harvested every two days. Cells will be counted to assess the effect of the antibody, and hypothesized neutralization of GRP on cell growth. Telomerase activity and free GRP assays will be repeated as described above. The GRP RIA will be done to ensure that GRP has been bound by the monoclonal antibody. As before, conditioned media from each data collection point (days 0, 2, 4, 6, and 8) will be collected, and processed with size exclusion spin filters. Any GRP bound to antibody will be retained by the 10 kDa filter, and only unbound GRP will be in the filtrate. The filtrate will be assayed in the RIA. This experiment will be repeated three times.

Experiment Three -The effect of additional GRP will be investigated. Three different types of GRP will be examined, the 27 amino acid full length GRP, and two peptide fragments, GRP 1-16, and GRP 14-27. Cell lines will be cultured in increasing concentrations of GRP (2x, 5x, 10x) added to the culture media. Cells will receive fresh GRP and media every two days, and cells harvested on days 0 (control), 2, 4, 6, and 8. GRP Telomerase assays will again be repeated as previously described. This experiment will be repeated three times.

Statistical Analysis - Repeated measured analysis of variance will be used to examine the effects of antibody 2A11 and GRP peptides on cell growth, telomerase activity and GRP concentrations. All data will be compared to the control day. In addition data will be analyzed within day to determine differences in effect of peptide concentrations on the above parameters.

**Progress:** All work has been completed on this protocol. Data analysis is currently underway.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/099

**Status:** Terminated

**Title:** Postoperative Cisapride Therapy After Abdominal Surgery in the Pediatric Patient

**Principal Investigator:** CPT Leroy J. Trombetta, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Tommy A. Brown, MC; LTC Kenneth S. Azarow, MC; COL James M. Noel, Jr., MC; LTC David Wiechmann, MC

**Start Date:**  
8/20/1998

**Est. Completion Date:**  
Jul 99

**Periodic Review:**  
7/27/1999

**Study Objective:** To compare the effects of cisapride and erythromycin on return of bowel motility and length of hospital stay in pediatric post-surgical patients.

**Technical Approach:** Subjects will be randomized in one of two groups. Group A will receive erythromycin at 1-3 mg/kg orally TID and Group B will receive cisapride 0.2 mg/kg orally TID. The medications will be placed in a medication syringe labeled "Trombetta study med" to prevent identification by nursing and physician staff. Subjects will take the study medication until time of discharge. Information will be collected concerning length of hospital stay, onset of bowel movements, regular diet and intake and perioperative complications.

**Progress:** The PI requested this protocol be terminated, 7 Jul 00, due to a lack of eligible subjects.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/086	<b>Status:</b> Ongoing
<b>Title:</b> Telomerase Enzyme Activity in a Metastatic Neuroblastoma Nude Mouse Model		
<b>Principal Investigator:</b> CPT Leroy J. Trombetta, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT James A. Sebesta, MC; M. J. DeHart, B.S.; Robert S. Sawin, M.D.; CPT Jeffrey A. Vos, MC; Cynthia Pekow, Ph.D.; LTC Kenneth S. Azarow, MC		
<b>Start Date:</b> 9/28/1999	<b>Est. Completion Date:</b> Apr 00	<b>Periodic Review:</b> 9/14/2001

**Study Objective:** To evaluate telomerase activity in human neuroblastoma tumors grown in nude mice, with attention to the difference in telomerase activity between primary tumor and metastases.

**Technical Approach:** Telomerase activity will be determined using the telomere repeat amplification protocol (TRAP assay). Data to be collected and analyzed includes: 1) Telomerase enzyme activity level represented by the absorbance values obtained from the TRAP-ELISA. Telomerase activity of the in vitro cell line, primary subcutaneous tumor, and metastatic foci will be compared; 2) Histologic analysis of neuroblastoma cell line, primary tumor and metastatic foci will be compared.

**Progress:** No work has been initiated on this study in FY00.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 200/021

Status: Ongoing

**Title:** A Multicenter Trial of Adjuvant Interferon Alpha-2b for Melanoma Patients with Early Lymph Node Metastasis Detected by Lymphatic Mapping and Sentinel Lymph Node Biopsy

**Principal Investigator:** COL William C. Williard, III, MC

**Department:** Surgery/General Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Alan L. Beitler, MC; MAJ David E. McCune, MC

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Jan 12

**Periodic Review:**  
N/A

**Study Objective:** (1) Determine whether regional lymphadenectomy plus adjuvant high dose interferon alpha-2b therapy improves disease-free and overall survival for melanoma patients with early (sentinel lymph node-only) nodal metastasis detected by histology or immunohistochemistry, compared to lymphadenectomy alone, (2) Determine whether regional lymphadenectomy plus adjuvant high dose interferon alpha-2b improves disease-free and overall survival for melanoma patient with lymphadenectomy alone, (3) Determine whether lymphadenectomy alone improves disease-free and overall survival for patients with submicroscopic (detected by PCR only) sentinel node metastasis, compared to observation, (4) Determine the natural history (recurrences and survival) of patients with submicroscopic (detected by PCR only) sentinel lymph node metastasis, (5) Determine the positive and negative predictive value of RT-PCR analysis of sentinel lymph nodes to identify patients at risk for recurrence and death, and (6) Determine the positive and negative predictive value of RT-PCR analysis of peripheral blood to identify patients at risk for recurrence and death.

**Technical Approach:** All patients 18 to 70 years old with melanoma  $\geq$  1.0 mm Breslow thickness, no evidence of distant metastasis by history and physical examination, chest x-ray and liver function tests, and no palpable regional lymph nodes will be eligible, provided that the other entry criteria have been met. The Sunbelt Melanoma Trial is divided into 2 separate protocols, plus a preliminary trial. Protocol A includes patients with histologically or immunohistochemically positive sentinel nodes. Protocol B includes patients with histologically and immunohistochemically negative nodes, and PCR positive sentinel nodes. Patients with negative sentinel nodes (PCR, histologically and immunohistochemically) will be observed

After consenting into the preliminary trial, patients will be registered into the study. Lymphatic mapping and sentinel lymph node biopsy will be performed. A portion of each sentinel node will be frozen and stored for PCR analysis at a later time. The remaining lymph nodes will be sent for routine histology &/or serial sectioning and immunohistochemical staining

Patients eligible for Protocol A will sign a new informed consent form. A peripheral blood specimen for PCR analysis will be obtained. All Patients will undergo regional lymph node dissection. Patients with 1 positive sentinel node will be randomized to receive either observation or high dose adjuvant interferon alpha-2b therapy, with stratification by Breslow thickness and the presence of absence of tumor ulceration. If the patient has more than one positive sentinel node, any evidence of extracapsular extension of tumor or any non-sentinel node that is positive for metastatic melanoma will not be randomized, but will be treated with standard therapy. These patients will be followed to determine the predictive value of prospective peripheral blood PCR analysis for survival and recurrence. This group of patients also will be eligible to go off study and participate in other protocols if desired

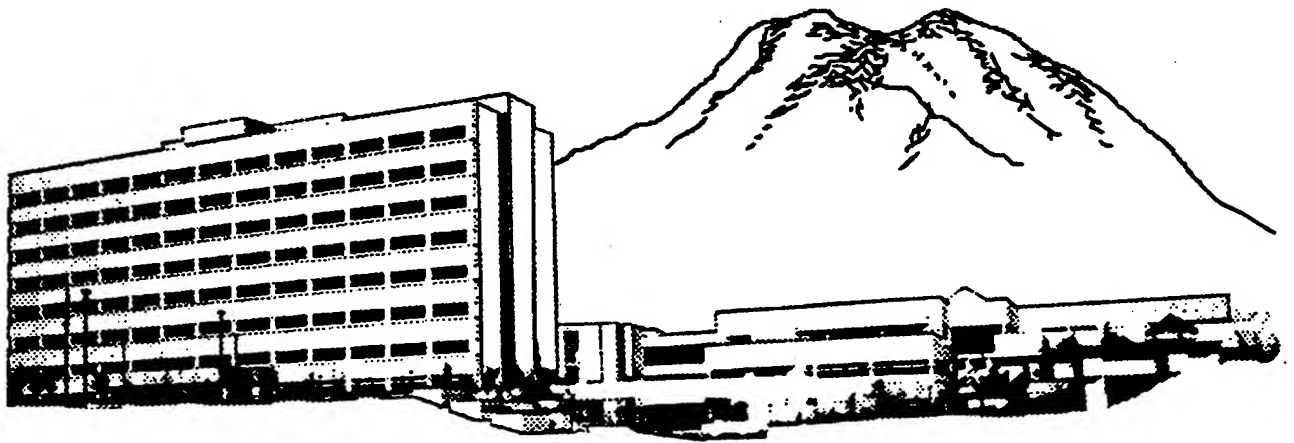
Patient eligible for Protocol B will sign a new informed consent form. A blood sample will be collected for eventual PCR testing, and will be randomized into 1 of 3 treatment arms: observation, lymph node dissection, or lymph node dissection plus one month high dose interferon treatment. These groups will be stratified by Breslow thickness and the presence/absence of ulceration

All patients will be followed, per standard of care, for up to 10 years, including, but not limited to, a visit every 3 months for years one and two, every 4 months for year three, every 6 months for years four and five, and yearly thereafter. Peripheral blood will be obtained for PCR analysis upon entry into Protocols A or B, at the 3 and 12 month postoperative visits, and yearly thereafter. Chest x-ray and liver function tests will be obtained annually per standard of care

Lymph node tissue is to be sent to the National Genetic Institute for immediate PCR testing of submicroscopic sentinel node metastasis to determine protocol A or B eligibility. The peripheral blood samples will be stored at the NGI until PCR testing can be conducted; as these tests are tangential to the study and can be completed as time permits. All tissue and blood samples will be destroyed upon closure of the study and not stored for future genetic research.

**Progress:** No patients have been enrolled in this study in FY00 at MAMC. The study remains ongoing for patient enrollment.





## **Detail Summary Sheets**

Ophthalmology Service,  
Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/034	<b>Status:</b> Ongoing
<b>Title:</b> Refractive Changes in a Low-tension Oxygen Setting Following Placement of Intracorneal Ring Segments		
<b>Principal Investigator:</b> CPT Steven M. Brady, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Larry White, M.D.; COL Vernon C. Parmley, MC; COL Thomas H. Mader, MC; MAJ Mark L. Nelson, MC; Troy H. Patience, B.S.		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Apr 00	<b>Periodic Review:</b> N/A

**Study Objective:** To observe changes in corneal shape and visual acuity that may take place in subjects exposed to low oxygen tension environments more than one month following the placement of intracorneal ring segments.

**Technical Approach:** This protocol will evaluate 20 subjects with intracorneal ring segments (ICRS) in a low tension oxygen setting. Refractive changes and corneal topography in subjects who have undergone ICRS implantation and who have been exposed to a controlled low-tension oxygen setting (via airflow restrictive goggles) for 2 hours will be compared to myopic controls who have experienced the same low-tension oxygen goggle system. Results will be compared to others who are exposed to altitudinal changes known to affect corneas who have undergone various keratorefractive procedures.

**Progress:** Four subjects have been enrolled in this study at MAMC during FY00. No significant data analysis has been possible due to low enrollment. Two subjects remained stable after the induced hypoxia while the other two subjects had changes in refraction. Subject recruitment continues.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 99/041

Status: Terminated

Title: Refractive Changes Due to Hypoxia Following Cataract Surgery

Principal Investigator: CPT David M. Bushley, MC

Department: Surgery/Ophthalmology Surgery

Facility: MAMC

Associate Investigator(s): COL Thomas H. Mader, MC; MAJ Mark L. Nelson, MC; MAJ Keith F. Dahlhauser, MC; Troy H. Patience, B.S.

Start Date:  
2/23/1999

Est. Completion Date:  
Jun 99

Periodic Review:  
N/A

**Study Objective:** The purpose of this study is to observe and compare changes in corneal shape and visual acuity that may take place in subjects more than 1 month following cataract surgery using a clear corneal or sutureless scleral tunnel incision, when their corneas are exposed to a low oxygen tension environment.

**Technical Approach:** We will select three study groups for our experiment. Group 1 will consist of volunteers who have had sutureless scleral tunnel incision cataract surgery. We will study several ocular parameters on these individuals, both prior to corneal exposure to hypoxia and immediately after two hours of corneal exposure to pure nitrogen (0% O<sub>2</sub>) gas via a goggle apparatus in one eye. The other eye will be exposed to compressed air (20% oxygen) as a control. These parameters include cycloplegic refraction, intraocular pressure, corneal video keratography, and central corneal thickness. Group 2 will consist of an equal number of subjects who have had clear corneal incision cataract surgery, in whom the same parameters will be monitored both pre and post corneal exposure to a hypoxic environment. Group 3 will consist of normal controls that have had no cataract surgery. The three groups will be age and gender matched.

Baseline evaluation of the subjects will include visual acuity, cycloplegic refraction 30 minutes after installation of one drop of 1% cyclopentolate, video keratography (corneal curvature mapping), central corneal pachymetry (thickness measurements), and intraocular pressure. One drop of proparacaine will be instilled into each eye prior to corneal pachymetry and measurement of the IOP. The same examiner using the same instruments will obtain all measurements.

The study will entail a one day process. On that day, baseline measurements will be obtained. Following baseline measurements, the subjects will be fitted with a pair of air-tight goggles. Compressed air will be released into one side of the goggles and 100% nitrogen will be released into the other after being bubbled through sterile water for humidification. Following two hours of exposure to these environments, the goggles will be removed and repeat measurements will be obtained immediately and again two hours post exposure. The examiner will be blinded to the type of gas to which each eye has been exposed.

The method of data analysis will be a multivariate analysis using repeated measures ANOVA. We will be comparing changes in corneal thickness (pachymetry), keratography, cycloplegic refraction, and visual acuity between baseline measurements and those obtained following corneal exposure to two humidified gas mixtures in Group 1, Group 2, and Group 3 patients, and between Group 1, 2, and 3 patients.

**Progress:** This protocol has been terminated by the PI due to insufficient time to conduct the study. 1 patient was enrolled in FY99, with inconclusive results. No work was conducted in FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/017	<b>Status:</b> Terminated
<b>Title:</b> Activated Protein C Resistance in Ophthalmologic Ischemic Syndromes		
<b>Principal Investigator:</b> CPT Benjamin B. Chun, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Mark L. Nelson, MC; MAJ Mary B. Grazko, MC; LTC Thaddeus J. Krolicki, MC; COL Anthony R. Truxal, MC		
<b>Start Date:</b> 1/26/1999	<b>Est. Completion Date:</b> Jul 99	<b>Periodic Review:</b> N/A

**Study Objective:** To identify APC resistance in individuals that may have ophthalmologic ischemia associated with thrombosis, manifesting as Central Retinal Artery Occlusion and Pseudopapilledema.

**Technical Approach:** APCr will be examined in 80 consecutive subjects (40 subjects per group) who are diagnosed with CRAO and Pseudopapilledema in the Ophthalmology Department at Madigan. All subjects identified as have APCr will undergo a Factor V DNA mutation test as a confirmatory measure. If the Factor V DNA test confirms the APC resistance test, the subject will be referred to Hem/Onc services for further treatment. Data analysis will be mainly descriptive analysis along with chi-square to compare each group's incidence to the incidence in normal population.

**Progress:** This protocol has been terminated by the IRB due to the PCS of its original investigator and failure to assign a new PI.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/050

**Status:** Ongoing

**Title:** A Phase III Study of MDX-RA Compared with Placebo Administered in Patients Undergoing Phacoemulsification or Planned Extracapsular Extraction for Cataract

**Principal Investigator:** MAJ Keith F. Dahlhauser, MC

**Department:** Surgery/Ophthalmology Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL Vernon C. Parmley, MC; COL Thomas H. Mader, MC; MAJ Mark F. Torres, MC; CPT Benjamin B. Chun, MC; MAJ Mark L. Nelson, MC; CPT Keith J. Wroblewski, MC; MAJ Roger K. George, MC; COL Kevin J. Chismire, MC; COL Dennis R. Beaudoin, MS

**Start Date:**  
1/16/1998

**Est. Completion Date:**  
Apr 99

**Periodic Review:**  
1/25/2000

**Study Objective:** Describe and compare the safety of a single dose of the murine immunotoxin MDX-RA to placebo over a six-month period post-randomization, and to test the efficacy of MDX-RA by comparing the proportion of patients in the treated group to the proportion of patients in the placebo group who have had a visual acuity explainable YAG laser capsulotomy<sup>3</sup> by 24 months of follow-up.

**Technical Approach:** In Phase I, subjects will undergo a pre-operative screening evaluation period prior to eye surgery for inclusion into the study; within four weeks for ophthalmic evaluations and within 2 weeks for physical evaluation. In Phase II, subjects will undergo phacoemulsification or planned extracapsular cataract surgery and receive 100 units of MDX-RA or placebo. In Phase III, during the 24 month follow-up period, ophthalmic examination, concomitant medication use, and occurrence of adverse experiences will assess safety. Subjects will be monitored for the need of visual acuity explainable YAG laser capsulotomies as the primary efficacy variable.

**Progress:** Six patients have been enrolled in this study at MAMC and continue to be followed. One patient was hospitalized with respiratory distress; however this event was considered unrelated to study participation. This study is currently closed to patient enrollment. Amendment #4 was IRB approved, which extended the study period from 24 to 36 months.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/119	<b>Status:</b> Completed
<b>Title:</b> The Use of Photorefractive Keratectomy on Active Duty U.S. Army Personnel for the Correction of Myopia		
<b>Principal Investigator:</b> COL Thomas H. Mader, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Vernon C. Parmley, MC; Troy H. Patience, B.S.		
<b>Start Date:</b> 7/18/1997	<b>Est. Completion Date:</b> Dec 99	<b>Periodic Review:</b> 7/25/2000

**Study Objective:** To determine if excimer laser photorefractive keratectomy (PRK) is a suitable procedure for use on active duty Army personnel for the correction of myopia.

**Technical Approach:** Refractive surgery of myopia with the excimer laser is of current command interest because of its potential to be performance enhancing in myopic active duty soldiers. Many active duty soldiers have an interest in this surgery and may elect to have it performed by civilian ophthalmologists at their own expense. There has been no prospective Army study to evaluate the effect of myopic excimer laser refractive surgery on active duty soldiers and how it affects the soldier's ability to perform his duties. This study proposes to 1) recruit a cohort of myopic active duty soldiers who voluntarily agree to participate, 2) prior to any treatment, evaluate their vision and its impact on certain basic military performance standards (such as qualifying with an M-16 rifle), 3) treat the myopia in both eyes by surface ablation of the cornea with an excimer laser, and finally 4) follow and re-evaluate vision and performance standards on these individuals for at least two years after treatment to examine the effect of the surgery on performance. One of the purposes of this study is to evaluate the potential of using this procedure to treat myopic soldiers thereby improving their ability to function in a combat environment and improve mission efficacy.

**Progress:** This study was completed and the conclusions reported in the MAMC Annual Progress Report, FY 99.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/017

**Status:** Ongoing

**Title:** The Effect of Latanoprost on Basic Tear Secretion

**Principal Investigator:** CPT Clifton S. Otto, MC

**Department:** Surgery/Ophthalmology Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert A. Mazzoli, MC; COL Kevin J. Chismire, MC

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Jun 00

**Periodic Review:**  
N/A

**Study Objective:** To measure the difference in basic tear production before and after administration of topical latanoprost.

**Technical Approach:** After measuring the normal amount of tears secreted by subjects, each subject will have 0.005% latanoprost put into the conjunctival sac of the left eye. Tear secretion will again be measured. The subject will be sent home with instructions to put latanoprost into their left eye once a day for seven days. After seven days they will return and have their tear secretion rates measured as before. Patients will also return for a one-month follow up evaluation to detect any side effects from one week use of latanoprost.

**Progress:** One subject has been entered into this study in FY00 at MAMC. Subject enrollment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 200/117                      **Status:** Ongoing

**Title:** A Pilot Study on the Use of Laser Assisted In-Situ Keratomileusis (LASIK) versus Photorefractive Keratectomy (PRK) in Active Duty U.S. Army Personnel for the Correction of Myopia and Astigmatism

**Principal Investigator:** COL Vernon C. Parmley, MC

**Department:** Surgery/Ophthalmology Surgery                      **Facility:** MAMC

**Associate Investigator(s):** MAJ Keith F. Dahlhauser, MC; CPT Steven M. Brady, MC; MAJ Robert B. Carroll, MC; CPT Clifton S. Otto, MC; CPT William Lim, MC

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Dec 03

**Periodic Review:**  
N/A

**Study Objective:** The purpose of this study is to compare laser assisted in-situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) using the Summit® autonomous excimer laser system and the Bausch and Lomb Hansatome® keratome as surgical methods for treating myopia and astigmatism in active duty soldiers.

**Technical Approach:** Approximately five hundred subjects who meet the inclusion criteria and who are active duty Army personnel between the ages of 21-55 with non-flying duties will be invited to participate in this study. The Argon fluoride excimer laser (193nm wave length) will be used to reduce the myopia and astigmatism of spectacle or contact lens dependent soldiers according to standard nomograms build into the laser controlling software of the excimer. Central ablation diameter will be 6.5 mm. Preoperative Assessments: Clinical examination will include past ocular and medical history, eye surgery or trauma, current medications, possible allergies, and a review of previous examinations and refractions. Hard contact lenses must be removed four weeks prior to the examination, and soft contact lenses must be removed one week prior to evaluation. Pupil size, uncorrected and best corrected visual acuity, manifest and cycloplegic refraction, keratometry and corneal topography, intraocular pressure, slit lamp biomicroscopy, central pachymetry, dilated ophthalmoscopy, and glare contrast sensitivity will be completed during the preoperative assessment and at the third month and one year examination

Subjects must be available for one year follow-up. If the volunteer states his/her desire to participate in the study, the consent process will be completed and a surgical date scheduled. On the day of surgery, each subject will be randomized (computer generated randomization) to undergo either bilateral sequential LASIK or PRK. All postoperative examinations will be performed at Madigan Army Medical Center. The subject will be examined on day 1, day 3, day 7, 1 month, 3 months, 6 months and 1 year.

At the one-month, three-month and one year evaluations, subjects will complete a questionnaire that subjectively assesses quality of vision and satisfaction with the procedure, as well as their subjective assessment of their ability to perform in their MOS. At the one-week evaluation, subjects will also indicate number of days after the procedure before they could return to full duty. If they have not returned to full duty by the one-week evaluation, this will be noted with a comment to ask again at the one-month evaluation if the patient has returned to full duty. The questionnaire used in this study is patterned after the functional vision test used in prospective evaluation of radial keratotomy study and the VF-14 visual function test developed for assessing visual performance in patients with cataracts.

**Progress:** This study recently received IRB/CIRO approval and has been forwarded to USAMRMC for review and approval.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/052

**Status:** Suspended

**Title:** Correction of Low Myopia (-1.00 to -3.50 diopters) in Active Duty Personnel

**Principal Investigator:** COL Vernon C. Parmley, MC

**Department:** Surgery/Ophthalmology Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL Thomas H. Mader, MC; CPT David M. Bushley, MC; CPT Michael A. McMann, MC

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Jun 02

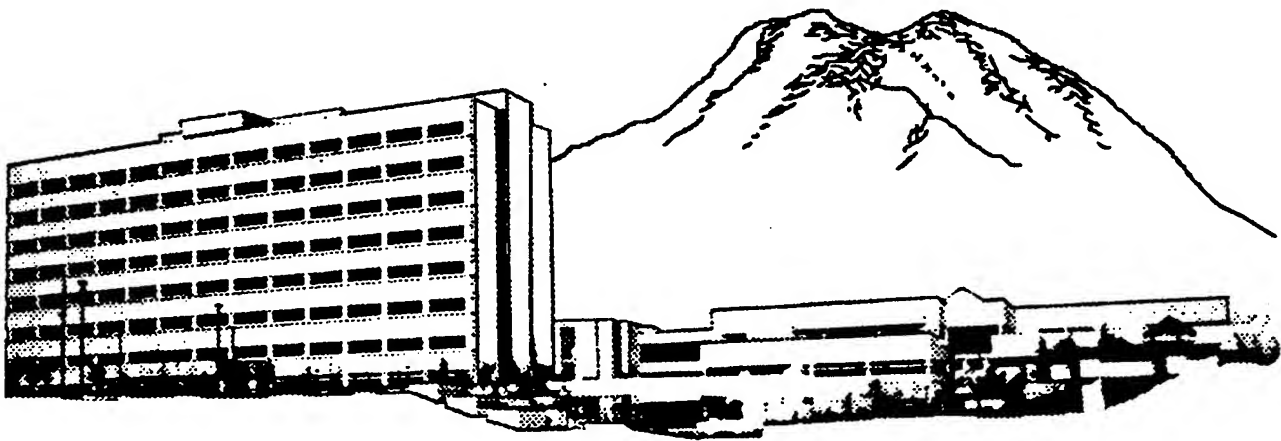
**Periodic Review:**  
3/28/2000

**Study Objective:** To determine the feasibility of correcting low myopia in active duty U.S. Army soldiers with the intrastromal corneal ring segment system (ICRS) developed by Keravision(r).

**Technical Approach:** We plan to recruit 100 patients into the study (200 eyes). Prior to performing the procedure, a baseline complete eye examination will be performed, including several tests of visual acuity. Pre and postoperative tests will also be conducted to determine the effect of the procedure on military performance. These tests will include M-16 weapons fire with and without protective mask, day and night navigation in good and inclement weather, and a subjective questionnaire on satisfaction with the procedure and symptoms associated with the procedure. The questionnaire will also address the effect on performance in the field after insertion of corneal rings.

The procedure involves inserting two small curved pieces of plastic into the stroma of the cornea, using a special trephine to create the stromal tunnel. The procedure can be done under topical anesthesia in the operating room (for sterility). The procedure takes approximately 15 to 20 minutes to perform. Evaluations will occur on postoperative day (POD) 1 and 6, and again at 1 month, 3 months, 6 months, and 1 year. If the patient consents, the second eye will be done 1 week following the first eye. The same postoperative follow-ups will occur for the second eye. Key data to be analyzed include: Post-operative visual acuity compared with pre-operative visual acuity; Post-operative refraction compared with pre-operative refraction, post-operative need for glasses; post-operative ability to perform specifically tested functions (weapons firing, ability to function in field without correction).

**Progress:** This study is currently suspended pending funding.



## Detail Summary Sheets

Orthopedics Service,  
Department of Surgery

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/095

**Status:** Ongoing

**Title:** Delayed versus Immediate Open Repair of Achilles Tendon Rupture; A Randomized Prospective Trial

**Principal Investigator:** CPT John Glenden Devine, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT George K. Bal, MC; LTC John D. Pitcher Jr., MC; MAJ Robert V. Williamson, MC; COL Frederic L. Johnstone, MC

**Start Date:**  
5/16/1997

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
7/25/2000

**Study Objective:** To evaluate the differences in surgically repairing Achilles tendon ruptures immediately, or waiting 10-14 days to perform the repair.

**Technical Approach:** All patients identified with acute Achilles tendon ruptures, who are being considered for surgical repair, will be presented the option of enrolling in this study. The subjects will be randomized to one of two Groups: Group I - Immediate surgical repair (within 72 hours) of the Achilles tendon, or Group II - delayed (between 10 and 14 days) surgical repair of the tendon rupture. The patients will be randomized using a computer generated randomization table. We will initially randomize the first ten patients, and a subsequent power analysis will be performed at 6 month follow-up to insure that enough patients are enrolled to make our results significant. The next 20 patients will be randomized using a second computer generated table. The post-operative course for both Groups will be the same. The patients will be followed up at 2 week, 6 week, 9 week, 6 month, 12 month, and 24 month intervals. They will be evaluated for post-operative complications and functional outcome.

**Progress:** 13 patients have been randomized in this study at MAMC. Data has also been collected on 14 patients who did not chose to be randomized or who could not be randomized because they presented after the acute period (within the first 72 hours); therefore, four groups will be compared. During FY00, only one of four patients consented to randomiztion. Two of those patients chose immediate repair and the third patient presented after 72 hours. All patients continue to be followed. Subject recruitment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/093      **Status:** Ongoing

**Title:** A Prospective Outcome Study of Posterior Lumbar Interbody Fusion in Soldiers

**Principal Investigator:** CPT Tad L. Gerlinger, MC

**Department:** Surgery/Orthopedic Surgery      **Facility:** MAMC

**Associate Investigator(s):** MAJ Robert W. Molinari, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Aug 00

**Periodic Review:**  
N/A

**Study Objective:** To determine the functional outcome and patient satisfaction of Posterior Lumbar Interbody Fusion (PLIF) in a military patient population.

**Technical Approach:** This prospective outcome study evaluates general health, pain, function and satisfaction in a consented patient population with degenerative disc disease. Patients will either elect to have posterior lumbar interbody fusion or not. Both groups will be given a validated outcome questionnaire at 3, 6, 12, and 24 months from when they elected to have the surgery or not. At 6, 12, and 24 months, patients will submit data from their PT tests. Results from both groups will be compared.

**Progress:** Six subjects have been enrolled in FY00 at MAMC. Subject enrollment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/081

**Status:** Ongoing

**Title:** A Prospective Randomized, Blinded Study, Comparing Treatment of Fifth Metacarpal Neck Fractures

**Principal Investigator:** CPT Tad L. Gerlinger, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL Frederic L. Johnstone, MC; Mary Miklos-Essenber

**Start Date:**  
5/22/1998

**Est. Completion Date:**  
Jun 00

**Periodic Review:**  
6/22/1999

**Study Objective:** To determine the effectiveness of treating fifth metacarpal neck fractures with closed reduction and casting with the metacarpal phalangeal joint in neutral and utilizing a three point mold.

**Technical Approach:** Patients with fifth metacarpal neck fractures will be randomized to undergo non-operative treatment, comparing closed reduction and casting with the metacarpal phalangeal joint in neutral and utilizing a three point mold, to closed reduction and casting with the metacarpal phalangeal joint approximating 90 degrees (the current standard technique). Outcome will be measured by the amount of residual angulation, grip strength compared to the contralateral hand, rotatory malalignment and range of motion at three weeks and again at three months after the injury.

**Progress:** Three subjects were enrolled in FY00, for a total of 6 patients. No adverse events have been reported. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/066	<b>Status:</b> Ongoing
<b>Title:</b> Healing of Stress Fractures Using Pulsed Electromagnetic Field (PEMF) Therapy		
<b>Principal Investigator:</b> CPT Karin A . Johnson, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC (Ret) Richard A. Sherman, MS; COL Nancy E. Henderson, SP; 1LT Kristine A. Youngstom, SP; Jerome Billingsley, M.D.; MAJ Susan Ishikawa, MC		
<b>Start Date:</b> 4/25/2000	<b>Est. Completion Date:</b> Dec 01	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether application of non-thermal, pulsed high peak power, high frequency, electromagnetic energy (PEMF) over the tibial stress fracture site used in conjunction with standard therapeutic approaches, reduces the amount of shin pain and increases endurance on the treadmill in relation to those receiving standard treatments with sham PEMF's.

**Technical Approach:** We propose to perform a double-blind, placebo controlled study of active duty soldiers but with tightly controlled outcome measures. All subjects will receive the standard treatment in addition to PEMF or sham and will begin participation within 30 days of initial complaint after confirmation of stress fracture diagnosis by both physical findings and bone scan. Prior to initial exposure, each subject will fill out a standardized questionnaire which assesses ability to function in the work and home environment in relation to lower limb pain and disability. Each will also be evaluated for duration of walking on a treadmill until discomfort to standardize assessment of pain and endurance, and will have their bone density measured. Subjects will be randomly assigned to be exposed to either a PEMF generator putting out actual fields or an inactive (sham) generator. This will be an entirely double-blind study as the subjects will not be able to tell which group they are in because the devices sound the same and because the patients cannot feel the machine operating. The physical therapy technician who operates the device will know which generator each subject is exposed to but will not know which generator is putting out actual fields and which is the sham. The physical therapists and physician doing the evaluations will have no idea which group the patients are in. The function questionnaire and the treadmill test will be repeated at the end of the two week exposure period and then four weeks and six months after. A power analysis shows that 33 subjects will be needed in each group assuming that the actual exposure group will do better than the placebo group (one-tailed test) and that an 80% chance of finding a difference between the two groups at a 0.05 level of significance is sufficient to perform the study. Eighty subjects will be recruited to begin the study to permit a reasonable 15% dropout rate.

**Progress:** Eight subjects were enrolled in this study in FY00 at MAMC. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/087	<b>Status:</b> Terminated
<b>Title:</b> Duplex Sonographic Analysis of the Common Femoral Vein in Non-Weight Bearing: Age Difference in Men		
<b>Principal Investigator:</b> CPT Bryant G. Marchant, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC John D. Pitcher Jr., MC; COL David F. J. Tollefson, MC; CPT Kurtis L. Kowalski, MC		
<b>Start Date:</b> 7/17/1998	<b>Est. Completion Date:</b> Jun 98	<b>Periodic Review:</b> 7/27/1999

**Study Objective:** To define the venous dimensions during a variety of lower extremity cast applications, body positions, and ambulatory activities in various age groups of men.

**Technical Approach:** 15 subjects will be enrolled in this study; 5 patients about 18 years of age; 5 subjects about 50 years of age and 5 subjects about 70 years of age, all of similar size and weight and of the same sex. Baseline measurements of the common femoral vein will be made with the subject supine, erect, ambulatory full weightbearing, partial weightbearing, and non-weightbearing with B mode Duplex ultrasound. A treadmill will be used for the ambulatory readings. Next, an ace wrap, a knee brace, Ted Hose and a standard below the knee lower extremity cast will be applied to the subject's right leg. The order of device application will be randomized. The measurements will be repeated. Finally, an above the knee cast will be placed on the right leg and the measurements will be repeated.

**Progress:** This protocol has been terminated by the IRB; since a new PI has not been designated since the PCS of its original PI in FY99.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 98/088      **Status:** Terminated

**Title:** Blood Flow in the Common Femoral Vein in the Erect Patient with the Application of Compressive Devices

**Principal Investigator:** CPT Bryant G. Marchant, MC

**Department:** Surgery/Orthopedic Surgery      **Facility:** MAMC

**Associate Investigator(s):** LTC John D. Pitcher Jr., MC; COL David F. J. Tollefson, MC; CPT Kurtis L. Kowalski, MC

**Start Date:**  
7/17/1998

**Est. Completion Date:**  
Jun 98

**Periodic Review:**  
7/27/1999

**Study Objective:** To study the changes in blood flow velocity in the erect patient with the use of compression devices.

**Technical Approach:** 10 subjects will be enrolled. Using a Doppler ultrasound, the blood velocity of the common femoral vein will be measured 1 cm proximal to the entry of the greater saphenous vein. The measurement will be made 5 times in the standing position during the expiration phase of the respiration cycle for each subject. A calf pneumatic intermittent compression device (PICD), a thigh high PICD, and a foot PICD will be placed on the patient and the velocity again measured during inflation and deflation of each SCD. Each measurement will be taken five times

The order in which the devices are placed on the leg will be randomized.

**Progress:** This protocol has been terminated by the IRB; since a new PI has not been designated since the PCS of its original PI in FY99.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 96/086

**Status:** Ongoing

**Title:** A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus A Cancellous Trough

**Principal Investigator:** LTC Patrick St Pierre, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** Hollis Potter, M.D.; CPT Roger W. Dougherty, SP

**Start Date:**  
3/15/1996

**Est. Completion Date:**  
Apr 99

**Periodic Review:**  
3/28/2000

**Study Objective:** To determine if tendon repair to a cancellous trough is necessary for rotator cuff repair in humans.

**Technical Approach:** Forty patients with proven rotator cuff tears will be randomized to two surgical groups. Group A will have their rotator cuff tendon repaired to the greater tuberosity after a trough is made in the greater tuberosity of the humerus. Group B will have their rotator cuff repaired to the cortical bone of the greater tuberosity of the humerus without the creation of a trough. A thorough debridement of soft tissue to include bursa and scar will be performed in both groups. Postoperative treatment will be the same for each group. Clinical evaluations and physical exams to include range-of-motion, shoulder impingement signs and tenderness will be performed at one, six, twelve and twenty-four month follow-ups by the physical therapist department. The modified Hospital for Special Surgery (HSS) Score as well as an analog pain, function, and satisfaction score will be used for clinical evaluation. A significant difference in the assessment of strength scores would indicate superiority of one method over the other. MRI evaluations will be performed at six, twelve and twenty-four months. The MRI will be evaluated by an MRI radiologist at the HSS in New York City, New York, who will be blinded to the method of treatment for each patient. Criteria for success by MRI has been established by a recent study performed at the HSS by the radiologist and the principle investigator.

**Progress:** Nine patients were enrolled during FY00, for a total of 22 patients enrolled in this study at MAMC. Follow-up continues on enrolled patients. No adverse events have been reported. No data analysis is available at this time.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 96/092

**Status:** Completed

**Title:** A Prospectively Randomized Study on the Effectiveness of Post-Operative Knee Bracing for Anterior Cruciate Ligament Reconstruction

**Principal Investigator:** LTC Patrick St Pierre, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Michael E. Kirk, MC

**Start Date:**  
4/19/1996

**Est. Completion Date:**  
May 99

**Periodic Review:**  
3/28/2000

**Study Objective:** The objective of this study is to compare the effect of different post-operative brace patterns on the final outcome of an anterior cruciate ligament reconstruction. This will be performed by prospectively randomizing patients into two different bracing groups and comparing them with subjective and objective testing during their rehabilitation period.

**Technical Approach:** In summary, the present knowledge on post-operative bracing for ACL reconstruction is limited. This study is designed to determine if post-operative bracing has an effect on the outcome of an ACL reconstructed patient. A total of 80 patients will participate in the study. After arthroscopically assisted ACL reconstruction patients will be randomized to two study groups. Group A will wear a knee immobilizer for three weeks after surgery followed by no protective bracing for the remainder of their rehabilitation. Group B will wear a Don-Joy IROM brace locked at 0 degrees for three weeks followed by three weeks in the brace with flexion set to 10 degrees less than maximum flexion. At six weeks, the patient will wear a Don-Joy off-the-shelf functional knee brace daily for six months and for vigorous activities after that for at least the first year. Data collected at one, two, six, twelve, and 24 months will include range-of-motion, Lachman, anterior drawer and pivot shift tests, as well as thigh circumference measurements. In addition at the six, twelve and 24 month follow-up visits, KT-100, LIDO, Lysholm and IKDC tests will be administered. A significant difference in the stability or functional assessment scores would indicate superiority of one method over the other regardless of cost. If both treatment groups are found to be equivalent, the most cost effective treatment method would be without bracing.

**Progress:** Subject enrollment has been completed with 55 subjects enrolled in this study at MAMC. No adverse events were reported. Final analyses are not yet available.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/065

**Status:** Ongoing

**Title:** Study of the Treatment of Articular Repair (STAR): A Prospective, Longitudinal Within Patient Evaluation of the Effectiveness (Durability) of Carticel (autologous cultured chondrocytes) Compared to Non-Carticel Surgical Treatment for Articular Cartilage Defects of the Knee

**Principal Investigator:** LTC Doug A. Vermillion, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Patrick St Pierre, MC

**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Jun 06

**Periodic Review:**  
N/A

**Study Objective:** To compare the effectiveness (durability) of Carticel autologous chondrocyte implantation in patients who have had an inadequate response to a prior non-Carticel surgical cartilage repair procedure (including debridement, microfracture, drilling, abrasion arthroplasty or other surgical treatment) within the previous 3 years for significant articular cartilage defects of the femoral condyle.

**Technical Approach:** This study will be a longitudinal, prospective, multicenter, within patient evaluation of 100 patients with articular cartilage defects of the knee who have had inadequate response to a prior non-Carticel surgical treatment. Patients who had an inadequate response to a prior non-Carticel surgical treatment will be implanted with Carticel (autologous cultured chondrocytes). the overall condition of the knee will be evaluated Using Modified Cincinnati Knee Rating System at baseline and every 6 months postoperatively. The SF-36 health survey will be used to assess global health status at baseline and follow-up visits. The primary endpoint of the study will be time to treatment failure, and will be compared via chart review of consented patients to the durability of past treatments.

**Progress:** One patient has been enrolled in this study in FY00 at MAMC. No adverse events were noted. Patient enrollment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 97/099      **Status:** Terminated

**Title:** Tendon-Healing to Cortical Bone After Tendon Reattachment Using Suture Anchors. A Biomechanical and Histological Evaluation in Goats

**Principal Investigator:** MAJ Robert V. Williamson, MC

**Department:** Surgery/Orthopedic Surgery      **Facility:** MAMC

**Associate Investigator(s):** LTC Patrick St Pierre, MC; MAJ Ronald E. Nielsen, VC; CPT Jason L. Blaser, MS; CPT Tad L. Gerlinger, MC

**Start Date:**  
4/25/1997

**Est. Completion Date:**  
Apr 00

**Periodic Review:**  
11/30/1999

**Study Objective:** To examine the biomechanical properties and histological appearance of the bone-tendon interface after rotator cuff tendon repair of the shoulder in goats. The tendon will be reattached directly to the outer surface of the bone (i.e. cortical bone) using four different types of commercially available suture anchors for fixation. This will test if the anchor properties have any effect on healing of tendon to bone after surgical repair.

**Technical Approach:** An experimental model using the infraspinatus tendon in goats for evaluation of tendon repair has been established. 36 adult (3-5 years old) goats, *Capra hircus*, will be treated with bilateral tenotomy and subsequent reattachment of the infraspinatus tendon. Each test goat will have different types of suture anchors used on contralateral shoulders. The study endpoint will be at six and twenty-six weeks following operative repair. A total of 40 animals will be assigned by randomized block design to the timing and sequence of the operative techniques, the types of fixation, and for biomechanical, histological or control testing. (e.g. The first animal may be randomized to have anchor #1 used in the left shoulder and anchor #4 used in the right. It may be randomized to the histological group. The second animal may be randomized to have anchor #2 used in the left shoulder and anchor #3 used in the right. It may be randomized to the biomechanical testing at 26 weeks). Thirty-six animals will be used for biomechanical testing and four for histological analysis. By performing bilateral procedures in the same animal, we will be able to use pairing to compare different methods of fixation. This increases the statistical power of the study and reduces the number of animals needed.

**Progress:** This protocol was terminated, 30 Nov 99, by the IACUC when it was determined during the semi-annual program review that a full quorum had not been present during the study's initial approval. The protocol had never been initiated and no animal use occurred on this study at MAMC as the investigators were seeking funding for the study.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/125

**Status:** Ongoing

**Title:** Subacromial Injection of Corticosteroids versus Ketorolac for Treatment of Shoulder Impingement Syndrome

**Principal Investigator:** MAJ Christopher J. Wilson, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** LTC Patrick St Pierre, MC; CPT Brian K. Konowalchuk, MC

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Jun 01

**Periodic Review:**  
N/A

**Study Objective:** To evaluate the difference in pain relief and functional outcome for subacromial impingement syndrome for patients who are treated with either a subacromial injection of corticosteroids or a subacromial injection of Ketorolac.

**Technical Approach:** This double-blind, randomized study will enroll approximately 40 patients with uncomplicated impingement syndrome for treatment with either subacromial corticosteroids or Ketorolac. Subjects with subacromial impingement will be given either 6cc 1% lidocaine with epinephrine and 40 mg Triamcinolone (Control) or 6cc 1% lidocaine with epinephrine and 60mg injectable Toradol (Test). Patient evaluation will be done at the time of injection and at 4 weeks post-injection.

**Progress:** Four subjects have been enrolled onto this newly approved study. Subject enrollment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/125

**Status:** Ongoing

**Title:** External Fixation of Displaced Clavicle Fractures

**Principal Investigator:** MAJ Christopher J. Wilson, MC

**Department:** Surgery/Orthopedic Surgery

**Facility:** MAMC

**Associate Investigator(s):** MAJ Greer E. Noonburg, MC; LTC Patrick St Pierre, MC; LCDR Clayton G. Turner, MC, USNR

**Start Date:**  
7/18/1997

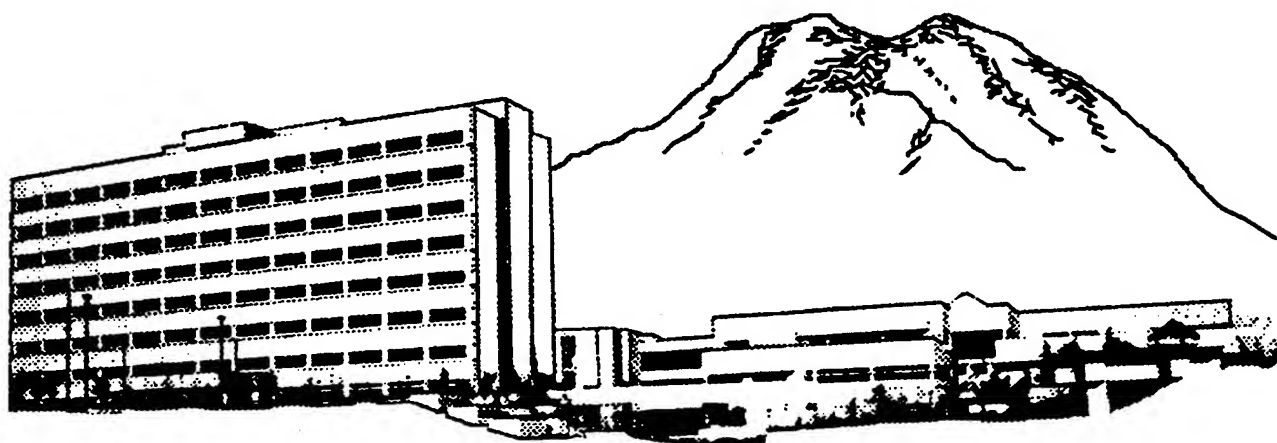
**Est. Completion Date:**  
Aug 99

**Periodic Review:**  
7/25/2000

**Study Objective:** Determine the efficacy of external fixation in the treatment of clavicle fractures with greater than 100% displacement.

**Technical Approach:** Patients will be drawn from males and nonpregnant females over age 18, with acute traumatic clavicle fractures having greater than 100% displacement on radiographs. The study population will range from 10 to 20 subjects. After inclusion in the study, and a pre-operative examination, the subjects will be taken to the operating room for placement of threaded pins through four 1-cm incision sites over the clavicle. An Orthofix Pennig II External Fixator will be attached to the pins and the fracture reduced to as close as possible to anatomic alignment. After surgery, the patient will be given pain medications, instructed in pin site care, and sent home. The patient will be evaluated weekly by an orthopaedic surgeon (4-8 weeks) and usually will receive clavicle x-rays with each appointment. The external fixator will be removed in the clinic in four to eight weeks, depending upon healing of the fracture as evident on x-ray. Subsequent post-operative exams at 3, 6, and 12 months will be conducted. Outcome variables will be evaluated for functional outcomes (motor strength, range of motion, tenderness at the fracture site, residual displacement/deformity, time of healing, ability to perform occupation and activities of daily living).

**Progress:** One subject has been entered in FY00 for a total of 19. MAJ Wilson assumed the role of PI due to the PCS of its original PI, Dr. Noonburg.



## Detail Summary Sheets

Otolaryngology Service,  
Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/068	<b>Status:</b> Ongoing
<b>Title:</b> Pharmacotherapy of Meniere's Disease. Project 1: Effects of General Anesthesia on the Vestibular System		
<b>Principal Investigator:</b> CPT James V. Crawford, MC		
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Vincent D. Eusterman, MC; George A. Gates, M.D.; JO Phillips		
<b>Start Date:</b> 4/27/1999	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> 9/26/2000

**Study Objective:** Document and quantify the extent of vestibular suppression after general anesthesia.

**Technical Approach:** The subjects will have an otologic history and then undergo an abbreviated rotating chair test. This non-invasive procedure is a standard clinical test and can be completed in 20 minutes.

The rotating chair is done using the Neuro-Kinetics equipment. The subjects is seated on a chair that rotates gently from the left to the right and back again in a sinusoidal manner at frequencies of from 0.01 to 0.64 Hz at a velocity of 60 degrees/sec. For the purposes of this research the test procedure will be limited to the 0.4 and 0.8 Hz frequencies, where the test-retest results are best. The test is done in the dark with the subject's eyes open after calibrating the system with standard gaze shifts. The resultant eye movements are recorded by skin surface electrodes and digitized, filtered, and the slow phase eye velocity is computed and stored. The average gain, phase, and asymmetry of the vestibulo-ocular reflex eye movements are computed for each test frequency and compared against age normals. A change in gain of 0.5 standard deviations averaged across the 0.04-0.08 Hz frequencies will be the key outcome parameter. Finally, the vestibular time constant will be determined from the time it takes the VOR to stop after a step deceleration of the chair.

To obtain 103 evaluable subjects, we estimate 130 people will need to be test preoperatively, expecting 10% to have abnormal vestibular tests and anticipating that 15 % will not complete the postoperative testing. About 95 % of the subjects are expected to be tested at MAMC, leaving an estimated 5 % to be tested at UWMC. An additional 10 control subjects will be tested at MAMC to ensure the test-retest reliability of our facilities.

**Progress:** One patient enrolled in this study in FY00 at MAMC. Subject recruitment continues.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/065	<b>Status:</b> Completed
<b>Title:</b> AlloDerm Tympanoplasty of Chronic Tympanic Membrane Perforations: An Animal Model		
<b>Principal Investigator:</b> CPT Timothy J. Downey, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Andrew B. Silva; CPT Anne L. Champeaux, MC; MAJ Larry K. O'Bryant, MC		
<b>Start Date:</b> 4/27/1999	<b>Est. Completion Date:</b> Mar 02	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether (1) chronic TM perforations can be created in chinchillas, (2) tympanoplasty success rates when using AlloDerm vs. fascia on chronic TM perforations in chinchillas, (3) histopathological integration of AlloDerm vs. fascia into the chinchilla TM after healed tympanoplasty of chronic TM perforations in chinchillas, and (4) there are complications of AlloDerm vs. fascial graft tympanoplasty on chronic TM perforations in chinchillas.

**Technical Approach:** This study will utilize 17 adult female chinchillas, weighing approximately 400-700 grams. One chinchilla will undergo an ear exam under anesthesia, transcanal creation of bilateral chronic TM perforations, harvesting of temporalis fascia, and then post-auricular approach underlay type I tympanoplasty of AlloDerm in one ear and temporalis fascia in the other. Since the TM perforations are acute, the animal will be euthanized at the end of these procedures. Approximately one week later, the remaining 16 chinchillas will undergo surgical creation of chronic TM perforations in both ears. All animals will undergo all procedures under general anesthesia. The ear canal will be sterilized with a povidine iodine solution, then irrigated several times with saline. The animal's sensorineural hearing will be unaltered.

Postoperatively, the chinchillas will be followed for 6 weeks. Ear exam under anesthesia (EEUA) will be performed weekly. Any debris or inflammatory tissue will be removed. If signs of TM healing are found (i.e. granulation tissue), the microflap procedure will be repeated. At 6 weeks, the EEUA will be repeated on all chinchillas. Those animals with closure of both TM perforations will be removed from the study. One chinchilla with a chronic perforation will be euthanized at this time and the TM will be harvested for histologic analysis. The remaining chinchillas with chronic TM perforations will be randomized before undergoing the following tympanoplasties: AlloDerm Tympanoplasty or Temporalis Fascia Tympanoplasty.

The chinchillas will be followed for 4 weeks. At this time, all will have an EEUA. Gelfoam will be suctioned from the external ear canals. One chinchilla from each group will be euthanized and their grafted TM's harvested for histologic analysis. At 8 weeks post-tympanoplasty (14 weeks post-perforation), all animals will be euthanized and then will undergo an EEUA with pertinent findings documented. Five animals from both tympanoplasty groups will have the grafted TM's harvested for histologic analysis. During each procedure, documentation will be done of any pertinent findings such as perforation size, granulation/inflammatory tissue, presence of infection, presence of cholesteatoma, graft breakdown, graft perforation, and surgical incision healing. Photodocumentation of the TM's will also be performed. One investigator will be blinded as to which graft material is present in each TM during EEUA. After resection the TM's will be marked for orientation and processed for paraffin embedding. Sections will be cut and stained with hematoxylin/eosin and trichrome. The tympanoplasty TM's will be examined for graft integration into the normal TM remnants and graft thickness. Documentation will be done of any inflammation, fibrosis, tympanosclerosis, epithelial hyperplasia, epithelial ingrowth, epithelial inclusion, or microperforations. The pathologists will also be blinded to the graft material in each TM specimen.

**Progress:** Bilateral perforations were made in the tympanic membranes of 17 chinchillas. At 4 weeks after tympanoplasty, 10 of 11 AlloDerm grafts and 9 of 10 fascia grafts had successfully closed the perforations. At 10 weeks, 9 of 10 AlloDerm and 9 of 9 fascia grafts were without perforations. The only AlloDerm failure was attributed to lateralization of the graft. Two animals were removed after developing postauricular wound abscesses that failed to resolve with appropriate treatment. An uncomplicated otitis media was discovered at 10 weeks in 2 of the AlloDerm animals. Histological analysis failed to show any significant differences in graft integration between the two groups. A statistically significant difference in reduced operative time in the AlloDerm tympanoplasty group (mean 47 minutes) was found when compared to the fascia tympanoplasty group (mean 68 minutes).

**Conclusion:** AlloDerm is a readily available material that is as successful as fascia for grafting chronic tympanic membrane perforations. The avoidance of donor site morbidity and of failure to breakdown during infection, as well as reduced surgical time allows AlloDerm to be a possible safe, cost-effective alternative to fascia. Further investigations are necessary in human trials.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/104

**Status:** Ongoing

**Title:** Measurement of Nasal Patency. Project 1: Measurement of Nasal Flow using Full-body Plethysmograph and Comparison with Visual Analog Scale

**Principal Investigator:** CPT John W. Hariadi, MC

**Department:** Surgery/Otolaryngology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paulino E. Goco, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jul 01

**Periodic Review:**  
N/A

**Study Objective:** Document nasal flow and resistance before and after application of Oxymetazoline Hydrochloride 0.05% and comparison with visual analog scale.

**Technical Approach:** Measure nasal flow volume loop using Sensormedics V6Z Autobox Full-body Plethysmograph. Data will be obtained by having subjects breathe through each nares individually, then through mouth as control. Subjects will have 2 cotton pledgettes soaked in oxymetazoline 0.05% placed in each nares for 15 minutes and the measurements repeated thereafter. Subjects also record a Visual Analog Scale before and after decongestion with oxymetazoline. This consists of a 100mm line marked with "extremely clear" at zero and "extremely blocked" at 100mm. The subjects are asked to indicate their subjective sensation of nasal congestion by marking the line for each nasal cavity, before and after application of the topical decongestant. Subjects use a 2x2 gauze to obstruct the contralateral nasal passage during assessment.

**Progress:** This study recently received final IRB approval. No work has been initiated on this study in FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/079      **Status:** Ongoing

**Title:** Determining Optimal Nonsurgical Treatment for Auricular Cartilage Contouring in a Rabbit Model

**Principal Investigator:** CPT Phillip L. Massengill, MC

**Department:** Surgery/Otolaryngology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paulino E. Goco, MC

**Start Date:**  
5/18/2000

**Est. Completion Date:**  
May 03

**Periodic Review:**  
N/A

**Study Objective:** To evaluate a potential nonsurgical technique for auricular contouring and to compare the results of auricular contouring with various proteolytic enzyme preparations (hyaluronidase, elastase, and relaxin) in combination with auricular splinting.

**Technical Approach:** Phase I (pilot phase) will utilize fresh slaughter house-derived (ex-vivo) rabbit ears randomly assigned to one of three treatment groups, Group 1 - hyaluronidase; Group 2 - elastase and Group 3 - relaxin. The ex-vivo ears will have varying concentrations or volumes of the specified enzyme injected into the auricular cartilage and will be mounted and weighted so as to allow gravity to bend the ears at the injected region if the cartilage is softened. Three ears each will be injected with each of three enzyme concentrations/volumes in each treatment group.

Evaluation for cartilage softening will be performed at 24, 48 and 72 hours postinjection and the solution concentration that allows the cartilage to maximally soften, without cartilage destruction, will be determined for each of the enzymes

Phase II will involve five rabbits for each selected enzyme volume/concentration. Rabbits will be placed under general anesthesia, with one ear injected with the test compound and the other ear injected with a volume of sterile, physiologic saline that is equal to the injected test compound volume. Following injection, both ears will be contoured manually, and molded with lightweight, Aquaplast splinting material. Rabbit ears will remain splinted for four weeks.

**Progress:** Phase II of this study has been partially implemented using a total of 10 rabbits and two different dose/concentration adjusted groups. Data collection is still underway. No data analysis is available at this time.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 99/050

Status: Ongoing

Title: Pediatric Bronchoesophagology Laboratory Using Swine (*Sus scrofa*)

Principal Investigator: MAJ Douglas Sorensen, MC

Department: Surgery/Otolaryngology

Facility: MAMC

Associate Investigator(s): Andrew Inglis, M.D.; MAJ Andrew B. Silva

Start Date:  
3/23/1999

Est. Completion Date:  
Mar 02

Periodic Review:  
5/18/2000

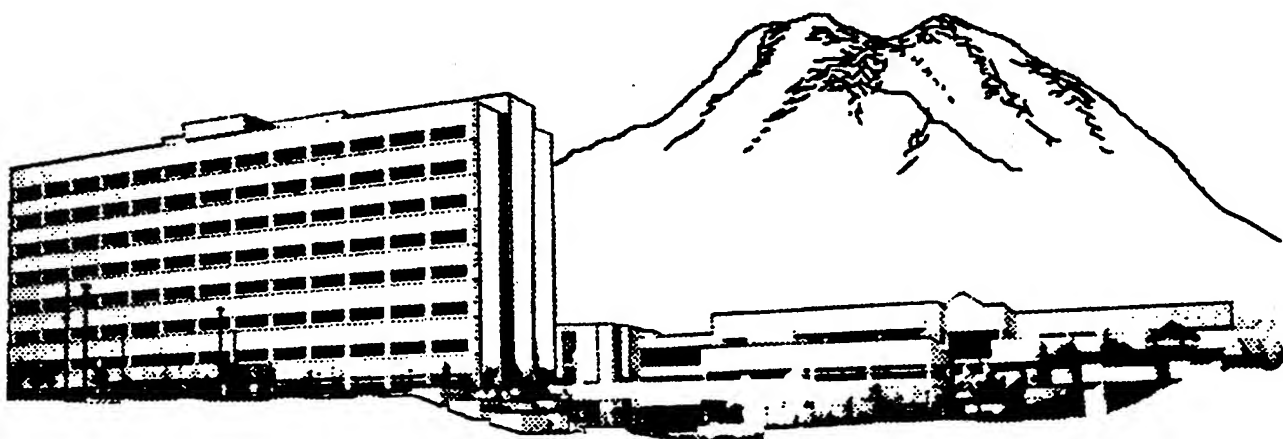
**Study Objective:** To familiarize the junior otolaryngology residents at MAMC and the UW and the Pediatric Surgery fellows at CHMC, with the endoscopic instrumentation and techniques required to evaluate and treat the tracheobronchial tree and esophagus in children. This would include familiarization with esophageal and tracheal foreign body removal, rigid and flexible endoscopic techniques and endobronchial laser use. Familiarity with these techniques would allow an increased margin of safety for children undergoing these procedures and better prepare the endoscopist to assist and then perform these procedures when necessary. Increased endoscopic training experiences will increase operative efficiency and minimize the potential operative risks involved in these procedures.

**Technical Approach:** This is a 4-hour afternoon laboratory session. The LARS, under the supervision of an attending veterinarian, will administer the anesthesia. During this time, 3 pigs will be anesthetized under general anesthesia using IM Rompun/ketamine (2.2mg/kg 20mg/kg). LARS will then obtain intravenous access. Once an adequate plan of anesthesia has been reached, the course participants will perform rigid and flexible bronchoscopy with extraction of a foreign body and esophagoscopy under the supervision of an attending endoscopist. In order to maximize the number of procedures that can be performed within the shortest amount of anesthetic exposure, three live animal stations will be used. The first and second station will be used to teach rigid endoscopy and foreign body removal. The third station will be used to teach flexible endoscopy and foreign body removal. There will also be two additional teaching stations. One will involve instrument set up and use, while the other will involve a teaching station for removal of a safety pin.

Approximately 20 endoscopic procedures will be performed on each animal. Foreign bodies will be used that reproduce those encountered in clinical practices (peanuts, beans, Lego). The foreign bodies will be endoscopically placed and extracted from the bronchus and trachea, under direct vision of the participants and instructors. At the end of the laboratory session, the pigs will be euthanized while they are still under general anesthesia in accordance with the IAW LARS SOP for euthanasia.

All course participants will perform bronchoscopies and foreign body removal on models prior to operating on the swine. The course participants will also participate in a half-day didactic component prior to the laboratory session and will be required to undergo a post course quiz. Completion of the training will be determined by the participant's ability to successfully, and atraumatically perform a bronchoscopy and esophagoscopy with airway foreign body removal.

**Progress:** One training session was held in FY 00; utilizing 2 pigs. The training lab was successful in allowing 10 residents the opportunity to sharpen their skills in bronchoesophagology. MAJ Douglas Sorensen assumed the role of PI for this study, Jun 00, at the request of the original PI, MAJ Andrew Silva.



## Detail Summary Sheets

Urology Service, Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/003	<b>Status:</b> Terminated
<b>Title:</b> Pilot Study to Determine the Inhibition of P-Fimbriated E. coli after Growth on a Cranberry Media			
<b>Principal Investigator:</b> MAJ Sunil K. Ahuja, MC			
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Andrew C. Peterson, MC; James R. Wright, M.T.			
<b>Start Date:</b> 10/26/1999	<b>Est. Completion Date:</b> Oct 99		<b>Periodic Review:</b> N/A

**Study Objective:** To determine the inhibitory potential of a concentrated cranberry product on the adhesive ability of p-fimbriated E.coli for human red blood cells.

**Technical Approach:** This study will grow known p-fimbriated E.coli which is exposed to a concentrated cranberry medium and examine the morphologic changes to the bacteria.

**Progress:** This protocol was reported as terminated, 31 May 00, due to lack of funding.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/019	<b>Status:</b> Ongoing
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**Title:** A Pilot Study of Radiofrequency Induced Coagulation Necrosis of Solid Renal Masses

**Principal Investigator:** LTC Raymond A. Costabile, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ David G. Omdal, MC

**Start Date:**  
11/19/1999

**Est. Completion Date:**  
Dec 04

**Periodic Review:**  
N/A

**Study Objective:** 1) To assess the capability of radiofrequency (RF) energy to induce a predictable zone of necrosis within renal tissue / tumor; 2) to determine the viability of cells within the zone of necrosis via pathological evaluation; and 3) to evaluate the response and follow up in patients who are not candidates for surgical resection of their solid renal masses.

**Technical Approach:** This prospective, nonrandomized study will treat various stages of renal cell cancer using radiofrequency (RF) induced necrosis of tumor tissue. The investigator will use ultrasound imaging to place an electrode into the affected tissue. The appropriate dose of RF energy will be released into the tissue in the immediate area. If the patient is a candidate for resection nephrectomy, the treated tissue will then be resected and assessed by pathological evaluation. After treatment, both groups will be followed and monitored to assess changes in the tumor and surrounding tissue.

**Progress:** Two subjects enrolled in this study during FY00 at MAMC; one in the ablation only arm and the other in the ablate and resect arm. Both subjects continue in follow-up without protocol induced complications. Subject enrollment continues.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/044		<b>Status:</b> Ongoing	
<b>Title:</b> Detection of Occult Metastasis in the Peripheral Blood of Prostate Cancer Patients					
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC					
<b>Department:</b> Surgery/Urology				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lisa M. Pierce, D.Sc.; MAJ Raymond S. Lance, MC					
<b>Start Date:</b> 2/22/2000		<b>Est. Completion Date:</b> Oct 01		<b>Periodic Review:</b> N/A	

**Study Objective:** To investigate the utility of several biomarkers for the detection of micrometastasis in the peripheral blood of patients with and without metastatic prostate cancer. Telomerase activity, human telomerase reverse transcriptase catalytic subunit (hTERT) mRNA expression and cytokeratin 19 (CK19) mRNA expression will be examined in circulating cancer cells.

**Technical Approach:** Subjects will be selected through the prostate cancer patient database existing in Urology Service, Department of Surgery, MAMC. Subjects will be divided into 5 groups of 25 patients each. Blood samples will be collected in tubes containing EDTA, subject identifiers will be removed and the sample assigned a number. A total of 23 ml of blood will be collected per subject; 4 x 5 ml tubes will be used for immunomagnetic enrichment with subsequent RT-PCR and telomerase activity assays and 1 x 3 ml tube will be used to separate serum for VEGF quantitation

Those samples undergoing immunomagnetic enrichment (4 tubes of 5 ml blood per patient), mononuclear cells (MNCs) will first be isolated from the anticoagulated blood. Each 5 ml blood sample will be layered over 5 ml of Histopaque-1077 solution in 15 ml tubes and centrifuge at 400 x g for 30 min at room temperature to separate the MNC layer from the red cells and plasma. These MNCs will be washed twice in RPMI 1640/5% FBS according to manufacturer's instructions and then will be resuspended in 1 ml phosphate buffer saline/1% FBS/0.6% NaCitrate. The epithelial cells will be harvested from these MNCs using 1 x 10<sup>7</sup> immunomagnetic beads coated with the epithelial-specific monoclonal antibody BerEP4. Bead-coated cells will be washed 3x in PBS/1% FBS/0.6% NaCitrate and then 1x PBS. Harvested epithelial cells then will be processed for hTERT, CK19 and B2-microglobulin mRNA expressions.

**Progress:** CK19 mRNA expression may be a useful biomarker to detect micrometastatic tumor cells in prostate cancer patients. Further investigation with greater numbers of cancer patients and controls is warranted. Telomerase activity and serum VEGF levels do not appear to be reliable biomarkers of occult metastasis in patients with prostate cancer.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/045	<b>Status:</b> Ongoing
<b>Title:</b> A Pilot Phase II, Placebo-controlled, Double-blind Study of KMD-3213 in patients with the Signs and Symptoms of Benign Prostatic Hyperplasia (BPH) Protocol #KMD-3213-US021-99		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Henry E. Ruiz, MC; CPT Cecily K. Peterson, MC		
<b>Start Date:</b> 2/22/2000	<b>Est. Completion Date:</b> Mar 01	<b>Periodic Review:</b> N/A

**Study Objective:** To test various aspects of KMD-3213 in patients with benign prostatic hyperplasia, including: (1) the most effective doses, (2) if the efficacy of KMD-3213 is maintained over time or if tolerance develops, (3) effects of KMD-3213 on vital signs in the target population, and (4) effects on electrocardiogram parameters, heart rate, and clinical lab tests in the target population.

**Technical Approach:** This multicenter, double-blind study will treat patients on one of three different treatment arms. After a 4-week placebo lead-in period, patients will be given either 0 mg, 4 mg, or 8 mg KMD-3213 to take daily for 8 weeks. At the end of the 8-week treatment period, efficacy of the drug will be assessed through uroflowmetry and questionnaires.

**Progress:** 17 subjects have been consented for this study, with 2 subjects randomized and 3 subjects in the washout phase. One patient experienced a mild decrease in orthostatic blood pressure and increase in heart rate post dose of blinded study medication. No SAEs have been reported, subject enrollment continues.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/087

**Status:** Ongoing

**Title:** Phase II Dose-ranging Study of HuKS-IL2 in Patients with Hormone Refractory Prostate Carcinoma

**Principal Investigator:** LTC Raymond A. Costabile, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Karen C. Evans, MC

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Jun 02

**Periodic Review:**  
N/A

**Study Objective:** (1) To evaluate the clinical activity of different dosing regimens of HuKS-IL2 by prostate-specific antigens (PSA) response, (2) To evaluate clinical activity by objective anti-tumor response, if applicable, (3) to determine the safety and tolerability of HuKS-IL2 administered at various drug levels and dosing schedules, (4) to evaluate the pharmacokinetics and immunogenicity of HuKS-IL2, (5) to evaluate the feasibility of different dosing regimens of HuKS-IL2, and (6) to compare the immunologic activity of different dosing regimens of HUKS-IL2 based on total lymphocyte counts, CD3+, CD4+, CD8+, CD19+, CD16+, and CD56+ cell counts.

**Technical Approach:** This open-label, dose-ranging study treats patients for 4 months and follows them for 4 weeks afterward. Patients will be treated with either 4mg/m<sup>2</sup> or 6mg/m<sup>2</sup> IV infusion on dosing days for 3, 4, or 5 consecutive days according to the assigned treatment cohort. Clinical activity will be determined by change in PSA, improvement in measurable disease sites, pain, and quality of life assessments.

**Progress:** This study recently received final IRB approval. No work has been initiated on this study in FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/103	<b>Status:</b> Ongoing
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**Title:** A Six-month, Open-label, Fixed-dose Study to Evaluate the Safety, Tolerance, Pharmacokinetics and Endocrine Efficacy of Two Doses of LA-2550 22.5 mg in Patients with Advanced Prostate Cancer

**Principal Investigator:** LTC Raymond A. Costabile, MC

<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC
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**Associate Investigator(s):** LTC Robert C. Allen, Jr., MC; MAJ Raymond S. Lance, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jul 01

**Periodic Review:**  
N/A

**Study Objective:** (1) To evaluate the safety and tolerance of two doses of LA-2550 22.5mg in patients with advanced prostate cancer, (2) To evaluate serum testosterone and LH levels following two doses of LA 2550 22.5mg in patients with advanced prostate cancer, and (3) To determine the pharmacokinetic (PK) profile of serum leuprolide acetate following two subcutaneous injections with LA 2550 22.5mg in a subset of patients with advanced prostate cancer.

**Technical Approach:** This open-label study will administer 2 subcutaneous injections of LA-2550 22.5 mg to patients with Jewett Stage C1, C2, D1, or D2 prostate cancer. The injections will be given at Day 0 and Month 3, with the patient returning daily and/or weekly for health assessment and blood sampling. Final assessments and evaluation will take place at Month 6. During participation in this study, patients will be monitored for safety through physical examination, vital signs, clinical laboratory values and adverse events.

**Progress:** Two subjects have been consented for this protocol in FY00 at MAMC, and are awaiting screening results. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/111	<b>Status:</b> Suspended
<b>Title:</b> A Phase III Crossover Study Evaluating the Efficacy and Safety of Uprima (Apomorphine HCl Tablets) Sublingual (2, 3, 4 mg) in Combination with Sildenafil Citrate (25 or 50 mg) in the Treatment of Male Erectile Dysfunction (#M00-181)		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Henry E. Ruiz, MC		
<b>Start Date:</b> 7/25/2000	<b>Est. Completion Date:</b> Sep 01	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to determine the safety and efficacy of Uprima (2, 3, 4, and 5mg) in combination with sildenafil citrate (25 or 50mg) compared with Uprima (2, 3, 4, and 5mg) alone and sildenafil citrate (25 or 50mg) alone in the treatment of patients with male erectile dysfunction.

**Technical Approach:** Subjects with erectile dysfunction will be randomized to receive medications on one of two arms of this study. Patients will be randomized to either arm and receive the following dosing combinations in any order:

Arm One: 2mg Uprima and placebo, 25mg sildenafil and placebo, or 2mg Uprima and 25mg sildenafil

Arm Two: 2mg Uprima and placebo, 50mg sildenafil and placebo, or 2mg Uprima and 50mg sildenafil

Patients and their wives/partners will both be required to sign consent forms. Diaries will be completed after each attempt at sexual intercourse. At office visits during the various periods of either arm of the study, both the patient and his partner will fill out questionnaires regarding erectile/sexual function. At the end of each treatment period, the subject will undergo a complete physical exam, ECG, and clinical lab test. The patient will wait between 48 and 96 hours to start the next period of the study. At the end of each period, both the patient and the partner/wife will fill out questionnaires (International Index of Erectile Function and Treatment Satisfaction Questionnaire for the patient, Brief Sexual Function Inventory and the Treatment Satisfaction Questionnaire for the partner.)

**Progress:** This study was terminated by the study sponsor in response to FDA concerns about the study methods; however, the study has been suspended at the request of the PI, pending FDA final decision and possible submission of an updated revised version.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/112      **Status:** Ongoing

**Title:** A Phase III, Randomized, Multicenter, Placebo-controlled, Double-blind, Clinical Trial to Study the Efficacy and Safety of CyPat (Cyproterone Acetate [CA]) for the Treatment of Hot Flashes Following Surgical or Chemical Castration of Prostate Cancer Patients and Its Impact on the Quality of Life in these Patients

**Principal Investigator:** LTC Raymond A. Costabile, MC

**Department:** Surgery/Urology      **Facility:** MAMC

**Associate Investigator(s):** MAJ Raymond S. Lance, MC; CPT Andrew C. Peterson, MC

**Start Date:**  
7/25/2000

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
N/A

**Study Objective:** To determine the efficacy of CyPat in the management of hot flashes in prostate cancer patients who have undergone bilateral orchiectomy or "medical castration" (LHRH agonist treatment)

To compare the effectiveness of the two doses (50 and 100mg) of CyPat for control of hot flashes

To determine safety (based on adverse events and laboratory parameters) of CyPat in the management of hot flashes in prostate cancer patients who have undergone bilateral orchiectomy or "medical castration" (LHRH agonist treatment)

To determine the impact of CyPat treatment on the quality of life in surgically or chemically treated cancer patients.

**Technical Approach:** After a one-week screening observation period, subjects will be randomized to receive either placebo, 50mg, or 100 mg of CyPat to control hot flashes. For 12 weeks, subjects will record incidence of hot flashes, and will periodically have checkups to ensure patient safety. Patients will complete quality of life questionnaires on a monthly basis during the treatment phase of this study. After the 12-week double-blind randomized part, eligible patients will have the option of continuing to take CyPat (100mg) for 6-9 months in an open label tolerability study.

**Progress:** This study recently received final IRB approval. No work has been initiated on this study in FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/140	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Multicenter, Phase III Trial Evaluating the Efficacy and Safety of BCI-ImmuneActivator (KLH) versus Adriamycin in BCG Refractory or Intolerant Patients with Carcinoma in situ with or without Resected Superficial Papillary Bladder Cancer		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC		
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> Jan 04	<b>Periodic Review:</b> N/A

**Study Objective:** To demonstrate the superior efficacy of BCI-ImmuneActivator versus Adriamycin (Doxorubicin Hydrochloride) in patients with carcinoma in situ (CIS) with or without resected superficial papillary bladder cancer who are refractory or intolerant to Bacillus Calmette Guerin (BCG) intravesical therapy and to evaluate the toxicity and safety of BCI-ImmuneActivator when administered intradermally and intravesically as compared to Adriamycin administered intravesically.

**Technical Approach:** This is a multicenter, prospectively randomized trial in patients diagnosed with CIS of the bladder with or without resected superficial papillary tumor, confirmed by biopsy within 3 months of study entry who have failed at least 1 course of BCG treatment or are intolerant of BCG therapy

Subjects randomized to the BCI-ImmuneActivator Arm will receive a sensitizing intradermal injection of BCI-ImmuneActivator about 2 weeks prior to receiving the study medication intravesically into the bladder. Subjects will then receive weekly instillations of study medication for 6 weeks. If they are complete responders at week 12, they will receive monthly therapy for 3 months. Partial or non-responders will receive weekly instillations for another 6 weeks, then if they become complete responders, will begin monthly treatments as above

Subjects randomized to the Adriamycin Arm will receive weekly Adriamycin intravesically into the bladder for 6 weeks. If complete response they will begin monthly installations for 3 months beginning at week 13. Partial or non-responders to Adriamycin will be withdrawn from the study.

All subjects will have cystoscopy every 3 months to evaluate response. At week 24, if complete response is noted, subjects will continue to receive monthly maintenance instillations of study drug or Adriamycin for another 6 months. Partial or non-responders will be withdrawn from the study.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/141	<b>Status:</b> Ongoing
<b>Title:</b> A Study Evaluating the Efficacy, Safety, and Tolerability of L-377202 in Bidimensionally Measurable, Androgen-Independent Prostate Cancer (Protocol No. 004-00)		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC		
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> Dec 02	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objectives of this study are to determine bidimensionally measurable disease radiologic response rates after treatment with L-377202 and to evaluate the general safety and tolerability of L-377202. The secondary objectives are (1) to determine bidimensionally measurable disease response rates (tumor burden, bone scan), (2) to evaluate PSA response rates obtained, (3) to evaluate pain and analgesic response rates, (4) to evaluate health-related quality-of-life responses, (5) to determine time to response, time to progression and response duration, (6) to determine duration of time during which patients maintain an ECOG performance status < 1, (7) evaluate 1 year cancer-specific and overall survival following treatment with L-333202, and (8) assess the effect of L-277202 treatment on biochemical markers of bone turnover.

**Technical Approach:** This is an open, nonrandomized study of male patients at least 30 years old with androgen-independent prostate cancer and bidimensionally measurable disease. After screening, eligible patients will be treated with a 30 minute infusion of L-377202, 225 mg/m<sup>2</sup> every 21 days. Each patient will be treated with at least 2 cycles, though additional cycles may be administered for stable or responding disease. Doses will be adjusted according to degree of myelosuppression experienced by each patient.

If a response or stabilization of disease is demonstrated, patients may continue to be treated for an indefinite number of cycles until either evidence of disease progression is documented, inclusion criteria can not be satisfied (except for PSA), or exclusion criteria are met. Assessments for disease progression must be performed every 2 treatment cycles. Pain will be assessed with the present pain intensity (PPI) scale of the McGill-Melzack Pain Questionnaire. Analgesic use will be assessed with the analgesic diary. Health-related quality-of-life will be assessed with the EORTC QLQ-C30 and the Osoba Quality-of-Life Module Prostate-14. The health economic impact of L-377202 will be assessed by collecting health resource utilization with the Health Economic Assessment case report form, which will be completed by the investigator or his designee. Duration of Time with an ECOG performance status < 1 is defined as the number of days during which a performance status of < 1 is reported.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/080	<b>Status:</b> Completed
<b>Title:</b> Phase III Randomized Study of a Single Adjunctive Instillation of Intravesical Valrubicin versus No Adjunctive Therapy Immediately Following Transurethral Resection in Patients with Multiple Superficial (Ta/T1) Bladder Tumors		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Bryon D. Joyner, MC; MAJ Raymond S. Lance, MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC		
<b>Start Date:</b> 7/27/1999	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> N/A
<p><b>Study Objective:</b> To assess the efficacy of a single 800 mg dose of intravesical AD-32 administered adjunctively, i.e., within two to twenty-four hours following a complete transurethral resection of presumed stage Ta or T1 bladder tumors, in 1) extending the time to recurrence in patients with Ta tumors; 2) reducing the rate of disease recurrence during the first 12 months following treatment in this patient population; 3) reducing the rate of and/or delaying the time to disease progression in patients with T1 tumors; 4) improving the outcome of patients diagnosed with stage T1 tumors and/or concurrent Tis [carcinoma in situ (Cis or stage Tis tumor)] treated subsequently with intravesical BCG therapy. Also, the toxicity of AD-32 treatment in this setting, including its effect on subsequent BCG immunotherapy, will be evaluated.</p> <p><b>Technical Approach:</b> This is an open-label, randomized, multicenter clinical study comparing adjunctive intravesical therapy with AD 32 immediately following a complete transurethral resection of bladder tumors (TURB) to TURB alone. Approximately 300 adult patients at 65 sites will be enrolled. Patients presenting with newly diagnosed or recurrent multifocal superficial transitional cell carcinoma of the bladder (<math>&gt;</math> or <math>=</math> two presumed stage Ta or T1 tumors) will be treated with complete TURB. Then, immediately prior to catheter removal, patients will be randomized to receive either a single adjunctive intravesical instillation of 800 mg AD 32 within 2 to 24 hours of resection, or no peri-surgical therapy. Patients will be observed for two hours after TURB whether or not they receive AD 32. Patients with T1 tumor(s) or concurrent Tis based on pathological analysis of biopsies performed at the time of surgery will receive immunotherapy with intravesical BCG starting <math>&gt;</math> or <math>=</math> 7 days but no later than 21 days after TURB (treatment schedule: six weekly instillations, a six week "rest period", and three additional weekly instillations). All patients will be followed at 3 month intervals until disease recurrence or progression, or for two years following treatment. Laboratory and diagnostic studies will be performed including medical history, CBC, serum chemistry, vital signs, physical examination and clinical observations for bladder symptoms, toxicities and adverse effects. Samples from all resected tumors and random biopsies will be analyzed locally to determine the pathological stage and histological grade of tumors; samples will also be reviewed by a central reference laboratory. All patients will undergo cystoscopy and cytology at each visit for 104 weeks (2 years) or until recurrence; in addition, patients determined to have Tis in post-surgical pathology analysis will undergo complete bladder mapping at the Week 13 evaluation and urine cytology analysis every 13 weeks for 104 weeks following TURB.</p> <p><b>Progress:</b> This study was closed to patient entry 16 Jun 00. Two patients were enrolled at MAMC; however, both patients were screen failures prior to receiving study drug.</p>		

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/089	<b>Status:</b> Ongoing
<b>Title:</b> Phase III Randomized, Double-Blind Study of DFMO vs. Placebo in Low Grade Superficial Bladder Cancer		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Robert C. Allen, Jr., MC; MAJ Bryon D. Joyner, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Mar 03	<b>Periodic Review:</b> 7/25/2000

**Study Objective:** To compare DFMO to placebo in patients with low grade superficial bladder cancers according to a) time to first recurrence of tumor, and b) toxicities.

**Technical Approach:** This will be a phase III randomized, double blind study of DFMO (an inhibitor of ornithine decarboxylase) versus placebo in low-grade superficial bladder cancers. Patients who meet the eligibility criteria will be stratified according to 1) history of newly diagnosed vs. recurrent; 2) stage Ta vs. T1; 3) grade 1 vs. grade 2; and 4) multifocal vs unifocal tumors. Then patients will be centrally randomized to receive either DFMO 1 gm/day or placebo, orally for 12 months in a double-blind fashion. Treatment will be discontinued in the presence of biopsy-proven recurrent disease, unacceptable toxicity, or patient refusal; however, every effort will be made to continue follow-up on these patients until the end of study. Patients will be followed with cystoscopy every three months for 2 years (every 6 months the 3rd year and annually for the 4th year). Based on 1.5 year enrollment and 3 year follow-up, study duration will be 5.5 years. CBC, including platelet count will be required within 12 weeks of randomization and at 6 months. An audiogram will be required at baseline and when indicated during the study. An independent pathologist will centrally review tumor specimens.

**Progress:** Three patients were enrolled in this study in FY00 at MAMC, and continue in follow-up. One patient complained of fatigue, which was thought to be possibly related to study drug. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/090	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Double-Blind Placebo-Controlled Phase III Trial Evaluating Zoledronate Plus Standard Therapy versus Placebo Plus Standard Therapy in Patients with Recurrent Carcinoma of the Prostate Who Are Asymptomatic with Castrate Levels of Testosterone and Have Rising PSA Levels Without Radiologically-evident Metastatic Disease		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Bryon D. Joyner, MC; MAJ Raymond S. Lance, MC; MAJ Sunil K. Ahuja, MC; LTC Robert C. Allen, Jr., MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC; MAJ Henry E. Ruiz, MC; MAJ David E. McCune, MC		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Oct 05	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** To determine if intravenous infusions with 8mg zoledronate is superior to placebo in the prevention of bone metastases.

**Technical Approach:** This is a prospective, stratified, randomized, double blind, placebo-controlled multicenter study in parallel groups. Five hundred prostate cancer patients with castrate levels of testosterone who are progressing biochemically by PSA only and have no radiologically evident metastases will be enrolled. Patients will be stratified according to the prior local treatment and the time interval between surgical castration or initiation of LHRH agonist and trial entry. Patients will receive double-blind study treatment until the development of bone metastases. After the development of bone metastases, all patients will receive open-label 8 mg zoledronate until the end of the study. Both the double-blind treatment phase and the open-label treatment phase have a fixed assessment schedule that must be followed. Once patients have completed the 48th month of the fixed assessment schedule, all patients will be followed for survival until LPLV (Last Patient Last Visit). LPLV for this study is defined as the time when the last patient completes the 4th month of study visit or has died. Assuming a placebo bone metastases-free survival rate of 20% at 2 years, this study is powered to determine if sequential infusion with 8 mg zoledronate administered every 4 weeks is superior to placebo in increasing the bone metastases- survival rate at 2 years to 32% (reduction of the hazard rate of bone metastatic disease in patients with prostate cancer by 29%). It is planned that the data from all centers that participate in this protocol will be combined, so that an adequate number of patients will be available for analysis. The Biostatistics department of Novartis will analyze the data from this study.

**Progress:** Ten subjects have been enrolled in this study in FY00 at MAMC. One subject complained of bone pain/myalgias, which was thought to be related to study drug. Multiple SAEs have been reported for renal insufficiency; the protocol was amended, Jul 00, in response to the SAEs. Subject enrollment continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/091	<b>Status:</b> Terminated
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**Title:** A National Phase II Trial of Intron Interferon (Alpha 2b) Plus BCG for Treatment of Superficial Bladder Cancer

**Principal Investigator:** LTC Raymond A. Costabile, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert C. Allen, Jr., MC; MAJ Raymond S. Lance, MC; MAJ Bryon D. Joyner, MC; MAJ Sunil K. Ahuja, MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
N/A

**Study Objective:** 1) To determine the clinical efficacy of combination BCG plus interferon-alpha 2b (IFN-alpha) immunology among various clinical subgroups with superficial bladder cancer including those that have failed prior therapy. 2) To determine the relative local and systemic toxicities of BCG plus IFN-alpha intravesical therapy and the effect on quality of life. 3) To determine the effect of BCG dose reduction during therapy on symptom tolerance and ability to maintain an extended treatment plan.

**Technical Approach:** The purpose of this study is to evaluate combination therapy for efficacy and toxicity in divergent groups of patients with superficial bladder cancer including those that have failed other forms of intravesical therapy. Depending on past history of BCG treatment and tolerance, patients will be enrolled into one of 3 arms for 6 weekly induction treatments: Arm 1 - full dose BCG for previously BCG untreated patients; Arm 2 - 1/3 dose BCG for prior BCG failures without intolerance; and Arm 3 - 1/10 dose BCG for BCG intolerant patients or those undergoing re-induction after prior BCG/IFN-alpha failure. The IFN- alpha (intron A) dose will be 50 million units (50 MU) in the first 2 arms and IOOMU in Arm 3. A maintenance program adapted from SWOG's successful 3 weekly mini-series regimen will involve 3 cycles given 3, 9, and 15 months after the end of the induction cycle

Toxicity and treatment tolerance will be determined based on patient symptom scores, a previously validated quality of life instrument, and clinician assessment. The use of BCG dose adjustment and/or delay or initiation of specific treatment will follow specific recommendations and results captured. Additional BCG dose adjustment may be permitted in special circumstances after approval from the National Principal Investigator. Premature termination of induction treatments will require study termination but abandonment of any or all maintenance treatments will not. Any tumor recurrence during the maintenance phase or any cancer progression will likewise require study termination. Patients with tumor recurrence after initial induction but before initiation of maintenance therapy may be re-treated in Arm 3. Treatment response will be assessed using standard of care bladder cancer monitoring every 3-4 months for 2 years with cystoscopy, urinary cytology, and biopsies when clinically indicated.

**Progress:** This protocol was terminated, 26 Oct 99, by the study sponsor before the study could be initiated at MAMC. Approval had been contingent on finding an acceptable pathway to acquire Intron for our patients within our health care system; however, efforts to accomplish this were unsuccessful.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/095	<b>Status:</b> Ongoing
<b>Title:</b> The Evaluation of Seminal Leucocytes and Cytokine Function of Infertile Males		
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start Date:</b> 8/24/1999	<b>Est. Completion Date:</b> Sep 01	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** To evaluate leucocyte function in infertile males and fertile controls.

**Technical Approach:** Patients seen in infertility clinic have a semen analysis as part of their routine evaluation. An aliquot of this semen analysis (approximately 10 microliters) will be cryopreserved in liquid nitrogen for immunohistochemical and microscopic (H&E) analysis for leucocyte, cytokine and germ cell composition and cataloging. Cell types will be counted on a hemocytometer to determine leucocyte composition after preferential staining with immunoreagents. Measurement of ROS by luminol florescence will be performed on fresh aliquots of semen specimens. Semen aliquots will also be obtained from patients undergoing vasectomy and vasectomy reversal. These aliquots will serve as controls (healthy, fertile males) and changes in leucocyte/cytokine composition before and after sterilization/reversal can also be documented. Semen analysis from vasectomy patients (known fertile controls) will be analyzed before and after vasectomy to establish mean populations of seminal leucocytes in healthy "normal" males. By measuring these populations before and after vasectomy, the testicular WBC contribution will be established. These "norms" of seminal WBC population can then be compared to infertility patients to evaluate any deviation in seminal leucocyte population. Immunoassays will be performed to measure levels of Interferon alpha, beta, gamma, as well as IL-2, IL-6 and TNFalpha. Additional cytokines may be measured as immunoassays are developed. Total seminal leucocyte count and differential seminal leucocyte count will be compared in infertile males and fertile male controls using the Student's two-sample t test to evaluate statistical significance. Seminal cytokine levels in fertile and subfertile males will also be analyzed using the Student's two-sample t test.

**Progress:** No work was done on this study during FY00.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 99/096                      **Status:** Ongoing

**Title:** Macroscopic and Microscopic Anatomy of the Arterial Supply to the Human Vas Deferens

**Principal Investigator:** LTC Raymond A. Costabile, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** None.

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
8/22/2000

**Study Objective:** (1) Describe the gross and microscopic blood supply to the vas deferens, (2) Assess the variability of the arterial and venous structures, (3) Assess collateral blood supply to the vas deferens, and (4) Utilize the new understanding of the vascular supply to improve operations on the spermatic cord, scrotal adnexa and vas deferens.

**Technical Approach:** Gross dissection of the, deferential blood supply: a) Gross dissection of cadaveric and specimens; b) Dissection of en bloc spermatic cord specimens from fresh and frozen cadavers; c) Microdissections on cadaveric specimens and autopsy specimens and recording of findings using photos and drawings. Microscopic description of deferential blood supply: a) Injection studies will be performed using India ink injections of the deferential artery, internal iliac artery and internal spermatic artery; b) Histologic sections will be performed using a dissecting microscope in the straight and convoluted portions of the vas deferens sagittally and transversely. These sections will be recorded using photomicrographs and drawings from medical illustrators.

The microscopic penetration of blood supply to human tissue does not lend itself to variability. The means by which arteries penetrate the wall of the vas deferens will likewise have minimal variability in normal vas deferens and deferential arteries. For this reason microdissection of 10 cadavers will give 20 examples of the method of penetration, providing more than 'adequate numbers for our purposes. The cadavers will be supplied from the Anatomical Teaching Lab at USUHS. They will either be fresh or frozen cadavers. A total of 10 cadavers will be required for this study.

Documentation of the blood supply to the vas deferens will be performed using photographs. Medical illustrations will be required since this is an anatomical study, pictures will be needed to present and/or publish data from this study. Medical illustrations will be done at the Graphics Department at USUHS or through the Graphics Department at HMJF.

**Progress:** No work was done on this study during FY00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/101		<b>Status:</b> Completed	
<b>Title:</b> A Six-Month, Two-Part, Sequential, Open-Label, Fixed-Dose Study to Evaluate the Safety, Tolerance, Pharmacokinetics and Endocrine Efficacy of Monthly Doses of LA-2500 in Patients with Advanced Prostate Cancer					
<b>Principal Investigator:</b> LTC Raymond A. Costabile, MC					
<b>Department:</b> Surgery/Urology				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Robert C. Allen, Jr., MC					
<b>Start Date:</b> 9/28/1999		<b>Est. Completion Date:</b> Oct 00		<b>Periodic Review:</b> 9/26/2000	

**Study Objective:** To evaluate the safety, tolerance, pharmacokinetics, and endocrine efficacy of monthly doses of a novel SC depot formulation of 7.5 mg leuprolide acetate (LA-2500) in patients with advanced prostate cancer.

**Technical Approach:** This is a multicenter, two-part, sequential, open-label, fixed-dose investigation of six monthly doses of LA-2500 administered to patients with Jewett Stage C1, C2, DI, or D2 adenocarcinoma of the prostate. A total of approximately 120 patients (30 patients in Part I and 90 patients in Part II) will receive a single, SC injection of LA-2500 every month (28 days) for six months. The study will be divided into two sections, Part I and Part II. During Part I, approximately 30 patients will be enrolled, given LA-2500, and evaluated. Twenty of the patients in Part I (denoted Group A) will have serum leuprolide acetate levels measured during the study for pharmacokinetic analysis. Once the 30 patients in Part I have completed through Day 42 (two injections of LA-2500), serum leuprolide acetate, T, LH, PSA, fractionated alkaline phosphatase, and safety data (including adverse experiences and safety labs) will be collated and summarized. While this analysis and summarization is being performed and reviewed, Part I patients will continue to be treated monthly with LA-2500 (provided that testosterone suppression is acceptable) and followed per the protocol. All Part I patients must complete through Day 42 (two injections) before Part II of the study can begin and the additional 90 patients enrolled. Both Part I and Part II patients will be followed for six months.

Descriptive pharmacokinetic parameters, including the maximum serum leuprolide concentration (C<sub>max</sub>), time of maximum serum concentration (T<sub>max</sub>), and area under the serum leuprolide concentration versus time curve for various time periods (0-28 days, 28-56 days, 56-84 days, and potentially other time intervals), will be determined. Observed values will be used for C<sub>max</sub> and T<sub>max</sub>. Area under the serum concentration versus time curve will be calculated using linear trapezoidal integration over the respective time limits. Plots of serum leuprolide concentrations versus time will be constructed for individual patients and for the mean values of all patients. The time scale for the plots will be selected to best present the observed data. Concentrations of serum leuprolide are expected to increase and vary somewhat within an initial equilibration phase, then approach a plateau. The time required to reach the plateau phase will be estimated from observed data. In addition the duration of measurable concentrations of serum leuprolide will be defined as the time of the last measurable serum leuprolide concentration. The steady-state average concentration during the plateau phase will be calculated as the area under the curve (AUC) for the plateau time interval divided by the duration of the plateau phase. Additional parameters or modifications of the stated parameters or analysis methods may be necessary to best describe the results.

**Progress:** This recently completed protocol enrolled 4 subjects during FY99 for a total of 6 subjects overall. Adverse reactions considered possibly related to study drug included two complaints of redness or itchiness at injection site and one complaint of hot flashes. Patients had a documented decrease in PSA and testosterone levels. The study sponsor has not yet completed their data analysis.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 94/051	<b>Status:</b> Completed
<b>Title:</b> Immunohistochemical Localization of Insulin-Like Growth Factor (IGF) Binding Proteins in Prostate Cancer		
<b>Principal Investigator:</b> MAJ Raymond S. Lance, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Stephen R. Plymate, M.D.; MAJ Richard R. Gomez, MC; CPT Michael D. Bagg, MC; CPT Patrick A. Twomey, MC; MAJ J. Brantley Thrasher, MC		
<b>Start Date:</b> 4/1/1994	<b>Est. Completion Date:</b> Jan 95	<b>Periodic Review:</b> 6/22/1999

**Study Objective:** The purpose of this study is to localize IGFBP's -2,-3,-4, and -6 in regions of histologically proven prostate cancer. Additionally, these same techniques weill be used to identify these binding proteins in areas of prostatic intraepithelial neoplasia (PIN) and benign prostatic hyperplasia (BPH). The information gleaned from this study will help better understand IGFBP expressin in both malignant, premalignant, and benign prostatic tissue.

**Technical Approach:** Radical prostatectomy specimens will be obtained by the Urology Service and taken to Pathology for histologic sectioning. Prostate adenocarcinoma will be identified in sections (as well as areas of PIN or BPH) with an adjacent section taken for immunohistochemical staining. Immunohistochemical staining will be performed for identification of IGFBP's-4, -2, -3, and -6 in regions of associated neoplams, PIN or BPH> Approximately 10 patients will be studied with comparisons to be made between neoplastic premalignant, and benign prostatic tissue.

**Progress:** Prostate tissue acquisition to complete IGF study of prostate cancer is complete. 24 samples were collected and studied. Data indicates that as human prostate disease tissue progresses from the benign to malignant state, insulin-like growth factor binding protein (IGFBP-2) immunoreactivity in the prostate luminal epithelial increases and IGFBP-3 decreases. Quantification in all cases was statistically significant. Additionally, no significant correlation was found between serum or tissue levels of PSA and IGFBP-2 or -3 immunoreactivity. Abstracts and articles resulting from this study are on file in DCI.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/104

**Status:** Ongoing

**Title:** Telomere Length and Telomerase Activity in Human Testicular Cancer

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** CPT Wade K. Aldous, MS; MAJ J. Brantley Thrasher, MC; MAJ Kenneth W. Westphal, MC; CPT Keith J. O'Reilly, MC; Troy H. Patience, B.S.; Lisa M. Pierce, D.Sc.

**Start Date:**  
6/16/1995

**Est. Completion Date:**  
Jul 97

**Periodic Review:**  
6/22/1999

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous testicular tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of testicular cancer.

**Technical Approach:** Tissue samples will be taken from 40 male patients undergoing surgical resection for testicular cancer. All malignant and benign tumor types resected during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to Rsa1 and Hinf1 restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into the telomere repeats on a known DNA primer. These will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress:** This study enrolled 2 patients during FY 00 for a total of 4 patients enrolled. Analysis of tissue is taking longer than originally planned due the rarity of tumor being studied.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/097

**Status:** Terminated

**Title:** Telomerase Activity in Voided Urine and Bladder Washings As A Diagnostic and Surveillance Marker for Transitional Cell Carcinoma

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ J. Brantley Thrasher, MC; CPT Wade K. Aldous, MS; CPT Jason L. Blaser, MS; Nan W. Kim; Judd W. Moul, M.D.; MAJ Steven Lynch, MC; LTC James P. Foley, CH; LCDR Christopher Kane, MC

**Start Date:**  
5/16/1997

**Est. Completion Date:**  
May 97

**Periodic Review:**  
5/25/1999

**Study Objective:** The objective of this study is to determine the sensitivity and specificity of telomerase activity in the voided urine and bladder washings of patients with bladder cancer as a diagnostic and surveillance marker. This will be compared to traditional cystoscopic examination.

**Technical Approach:** Bladder cancer remains a significant cause of cancer among both men and women in this country. Diagnosis and surveillance require invasive and often painful testing. Telomerase activity in the voided urine appears to be a promising non-invasive marker of bladder cancer. We seek to determine telomerase activity or its absence in the voided urine of 100 patients with newly diagnosed bladder cancer as well as approximately 200 patients at high risk for recurrence. We will compare these results to the telomerase activity in voided urine from 100 age matched, mixed gender subjects undergoing cystoscopy and found not to have bladder cancer. Data collected will include percentage of telomerase positive urine in the newly diagnosed bladder cancer group compared to the non-cancer control group. Furthermore the number of telomerase positive urine in patients with recurrent TCC in the group of patients at high risk for recurrent bladder cancer. Data will be analyzed to determine sensitivity, specificity, and positive predictive values.

**Progress:** This study was officially terminated, 31 Dec 99. Specimen processing does not allow for cell viability making telomerase activity a poor indicator in urine. Investigators were unable to develop a specimen processing method which will preserve cell viability to allow for telomerase as a marker for TCC. Results have been reviewed and submitted as a negative; not a clinically feasible testing method.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/147

**Status:** Ongoing

**Title:** Comparison of Quality of Life (QOL) Differences Between Radical Retropubic (RRP) and Radical Perineal Prostatectomy (RPP) for Clinically Localized Prostate Cancer

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ J. Brantley Thrasher, MC

**Start Date:**  
10/17/1997

**Est. Completion Date:**  
Sep 99

**Periodic Review:**  
9/26/2000

**Study Objective:** To determine QOL differences between patients undergoing RRP and those undergoing RPP for clinically localized prostate cancer.

**Technical Approach:** This study will prospectively evaluate and compare the QOL of male patients 30-80 years of age who undergo RRP and RPP for clinically localized carcinoma of the prostate. The study will utilize a validated questionnaire, the UCLA-RAND Prostate Cancer Index, administered to the patients (alone and without interruption) at least one week prior to the procedure and then at 1 month, 3 months, 6 months and 1 year postoperatively. This instrument will allow us to compare the effects of the 2 procedures on the patients' health-related QOL and eventually aid the urologist in choosing the appropriate approach for each patient.

**Progress:** This study is closed to patient entry; however it remains ongoing for follow-up. 236 patients were enrolled. Data has not yet been compiled or written in abstract form.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/092

**Status:** Ongoing

**Title:** Multicenter Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcomes, and Prognostic Analysis

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ J. Brantley Thrasher, MC

**Start Date:**  
7/17/1998

**Est. Completion Date:**  
Jan 13

**Periodic Review:**  
7/25/2000

**Study Objective:** Comprehensive longitudinal collection, maintenance and analysis of prostate cancer-specific and demographic standardized information from a large cohort of military health care beneficiaries from multiple geographically diverse health care centers.

**Technical Approach:** Standardized data collection instruments will be used at ten military medical centers by clinical research personnel and physicians to collect comprehensive prospective and retrospective information from men with prostate cancer. Patients will be followed proactively at a minimum of every twelve months until death. Data will be entered and maintained securely at USUHS in a relational database designed exclusively for this purpose. Standard statistical analysis will include survival analysis and univariate and multivariate analysis for prognostic factors.

**Progress:** Total number of subjects entered since protocol approval is 1210. A new database has been created and distributed to participating sites in an effort to provide a cohesive system for data collection. Also, an amendment was IRB approved, which now requires investigators to obtain informed consent for study participation. Newly diagnosed patients will be offered study participation prior to biopsy. Those subjects entered into the database prior to this amendment will be offered study participation during a follow-up appointment. Several patients entered previously declined consent and have been removed from the study.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/114

**Status:** Ongoing

**Title:** A Uniformed Services Comprehensive Database and Tissue Repository for the Study of Epidemiological, Detection, Natural History, and New Management Strategies for Prostate Cancer

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** LTC Stephen C. Groo, MC

**Start Date:**  
9/15/1998

**Est. Completion Date:**  
Jun 03

**Periodic Review:**  
8/22/2000

**Study Objective:** To establish a prostate cancer serum and tissue repository that will focus on the pathology and contain supportive clinical data for the study of the etiology of prostate cancer and will incorporate a demonstration project to illustrate the utility of the repository by examining interracial differences among men with prostate cancer.

**Technical Approach:** Subjects will be asked to allow the intraoperative collection of a blood sample, tissue biopsies of the excised organ and use of these specimens, as well as the retrieval and use of their original archival biopsy tissue. The sera and tissue will be tested for new markers in later studies to be conducted by both military and civilian prostate cancer researchers. Some of serum and tissue may be supplied to other research centers in the future.

**Progress:** Funding was just recently secured for this study. Work will be initiated once a coordinator is hired.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/003

**Status:** Ongoing

**Title:** A Randomized Double-Blind Comparative Trial of Bicalutamide (CASODEX) 150 mg Monotherapy Versus Placebo in Patients with a Rising PSA After Radical Prostatectomy for Prostate Cancer

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** Lori A. Loan, PhD

**Start Date:**  
10/20/1998

**Est. Completion Date:**  
Jan 01

**Periodic Review:**  
10/26/1999

**Study Objective:** (1) To compare bicalutamide 150 mg with placebo for time to treatment failure; (2) Quality of Life.

**Technical Approach:** Subjects will be randomized to receive either bicalutamide 150 mg daily or placebo until treatment failure, which is defined as an adverse event leading to withdrawal of randomized therapy, objective disease progression, death, initiation of systemic treatment or radiotherapy, or withdrawal from study therapy for any reason. Quality of Life data includes a PSA anxiety questionnaire (MAX-PC) and the FACT-P instrument, time to objective disease progression, PSA response, and time to PSA progression.

**Progress:** A total of 17 patients have been enrolled in this study at MAMC. Thirteen patients received study treatment, three patients withdrew prior to screening or receiving study drug and one patient was a screen failure. One patient died; however this death was considered unrelated to study participation. Twelve continue to be followed on this study.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/043      **Status:** Completed

**Title:** Liposomal Amikacin (MiKasome) in Complicated Urinary Tract Infections: Randomized, Double, Blind, Dose-Ranging Study

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert C. Allen, Jr., MC; MAJ Sunil K. Ahuja, MC; MAJ Bryon D. Joyner, MC; MAJ John B. Ellsworth, MC; CPT Keith J. O'Reilly, MC; CPT Karen C. Evans, MC; CPT Andrew C. Peterson, MC; LTC Raymond A. Costabile, MC

**Start Date:**  
2/23/1999

**Est. Completion Date:**  
Feb 00

**Periodic Review:**  
2/15/2000

**Study Objective:** To evaluate the safety and efficacy of three different doses of liposomal amikacin in the treatment of complicated urinary tract infections or acute uncomplicated pyelonephritis.

**Technical Approach:** A multicenter, double blind study of intravenous liposomal amikacin randomized between three fixed, single dose regimens. 165 evaluable patients will be enrolled and complete the study (55 evaluable patients per dose group). A maximum of 300 patients will be enrolled to obtain these 165 evaluable patients. Patients of either sex aged 18 years or older, with complicated urinary tract infections or acute uncomplicated pyelonephritis. The presence of at least one uropathogen at  $> 10^5$  CFU/mL will be required and patients with urinary catheters must be able to have these removed no more than 5 days after the start of therapy. Patients will be evaluated at Day 6, Day 14 (Test-of-Cure visit), Day 21, and Day 36 (Late Post-Treatment visit) after initiation of therapy. Efficacy endpoints will be microbiologic eradication and clinical cure assessed on each evaluation day. Safety assessments will include an evaluation of all adverse events spontaneously reported, elicited, or observed by the investigators including clinically significant laboratory test abnormalities.

**Progress:** This study was closed to patient entry 2 Feb 00, per the study sponsor. Ten patients were consented at MAMC; eight patients completed study treatment, 1 patient was lost to f/u, and 1 patient was a screen failure. All SAEs were reported to the IRB, including one adverse event with a MAMC enrolled patient. The event was felt to be unrelated to participation in the study.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/109

**Status:** Completed

**Title:** Limits of Serum Detection of Circulating Prostate and Bladder Cancer Cells using Telomerase Reverse Transcriptase (H-TERT) mRNA Detection by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)

**Principal Investigator:** MAJ Raymond S. Lance, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC; Amber J. Marean, B.S.; M. J. DeHart, B.S.

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
Apr 00

**Periodic Review:**  
N/A

**Study Objective:** To determine the methods necessary to detect circulating prostate and bladder cancer cells in human blood using highly sensitive techniques in preparation of testing in human prostate and bladder cancer patients.

**Technical Approach:** The human prostate cancer cell lines LNCAP and M12 and the human bladder cancer cell line T24 (all epithelial-derived cell lines) will be used for analysis in this study. Serial dilutions in phosphate buffered saline (PBS; 10, 20, 50, and 100 cells per 10 ml PBS) will initially be tested for telomerase activity using the telomere repeat amplification protocol (TRAP) assay (telomerase PCR ELISA kit, Boehringer Mannheim) and for H-TERT mRNA expression using RT-PCR (Perkin Elmer) including the appropriate positive and negative controls for these assays supplied in the assay kits. The cells will be prepared to a single cell suspension with 10 MM EDTA treatment instead of trypsin as trypsin removes the cell surface antigen necessary for the epithelial-specific BerEP4 antibody. RT-PCR to detect H-TERT mRNA expression will be performed using the primers and cycling conditions previously described by Ulaner et al. (1998). Telomerase activity will be measured according to the manufacturer's protocol.

In addition, serial dilutions of each of these cell lines will be spiked into 10 ml of volunteer whole blood (10, 20, 50, and 100 cells per 10 ml whole blood) prior to analysis for telomerase activity and H-TERT mRNA expression. Blood will be collected in 10 ml EDTA tubes to prevent coagulation. Heparin tubes will not be used because residual heparin may interfere with downstream RT-PCR applications. Fresh spiked whole blood (10 ml) will be layered over 10 ml Histopaque-1077 (Sigma) in 50" tubes and centrifuged at 400 x g for 30 min at room temperature to separate the mononuclear cells (MNCs) from the red cells and plasma. These MNCs will be processed according to the manufacturer's instructions and resuspended in 1 ml PBS/2% fetal bovine serum. The epithelial cells (spiked cancer cells and any normal epithelial cells from the volunteer blood) will be harvested from these MNCs using 10E7 immunomagnetic beads coated with the epithelial-specific monoclonal antibody BerEP4 (Dyna) according to the manufacturer's protocol using a magnetic field. Harvested epithelial cells (BECS) will be stored at -80°C prior to RT-PCR and TRAP analyses.

A subset of H-TERT RT-PCR assays performed on the HECs will utilize the Dynabeads mRNA DIRECT Micro kit (Dyna) for RT-PCR application. These oligo(dT)25 immunomagnetic beads are designed to rapidly isolate pure, intact polyadenylated mRNA ready for RT-PCR. The sensitivity of this mRNA isolation method will be compared to traditional total RNA isolation (Purescript RNA Isolation kit, Genta Systems) by examining the quality of the H-TERT RT-PCR results obtained by both methods.

Four vials of human volunteer blood will be collected per dilution of cells per cell line. For example, for the T24 cell line (as well as for the M12 and LNCAP cells), 4 vials (10 ml each) will be collected and spiked with 10 cells, 4 vials spiked with 20 cells, 4 vials spiked with 50 cells, and 4 vials spiked with 100 cells. Following the separation of the MNCs from all vials of whole blood, 2 of the 4 vials will be processed with immunobeads and 2 will not. H-TERT and TRAP ways (1 assay per



vial of spiked 10 ml whole blood) will be performed on HECs recovered using the epithelia-specific immunobeads as well as on the MNCs not processed with immunobeads. However, some "background" telomerase activity and H-TERT mRNA levels may be seen in the unprocessed MNCs due to the contaminating lymphocytes and stem cells which may possess low levels of telomerase activity and H- TERT mRNA. The number of specimens equals 3 cell lines (LNCAP, M12, T24) x 4 dilutions each (10, 20, 50, 100 cells) x 4 vials of blood per dilution (2 processed with immunobeads and 2 without immunobeads, 1 vial per TRAP assay and 1 vial per H-TERT assay) which is 48. In addition, several 10 ml vials of control, unspiked blood will be processed with and without epithelial-specific immunobeads and used in all experiments performed. An additional 4 vials will be collected and spiked with either 20 cells (2 vials) or 50 cells (2 vials) per 10 ml whole blood (only 1 cell line in this mini-experiment) to compare the immunomagnetic mRNA isolation and total RNA isolation methods prior to RT-PCR.

**Progress:** Results showed CK19 mRNA expression was detected in as few as 10 prostate (LNCaP, M12) or bladder (T24) cancer cells seeded into 5 ml blood. As negative controls, CK19 gene transcripts were not detected in volunteer blood spiked with 0 carcinoma cells or in isolated lymphocyte RNA. Increased telomerase activity was detected in 10-50 prostate and bladder cancer cells spiked into 5 ml volunteer blood when compared to control samples spiked with 0 cells. Telomerase activity levels increased in a dose response manner dependent upon the number of cells seeded into the blood samples. Controls (0 spiked cells) possessed low levels of telomerase activity similar to values achieved by 10 spiked cells.

Conclusions of this study are that low numbers of prostate or bladder carcinoma cells can be detected in the blood using immunomagnetic enrichment followed by CK19 nested RT-PCR or telomerase activity assays. CK19 mRNA expression may be a more sensitive (in that this method can detect fewer carcinoma cells) and specific biomarker of micrometastasis than telomerase activity levels. These results have important implications for continuing the investigation in vivo in prostate and bladder cancer patients at various stages of disease.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/026	<b>Status:</b> Ongoing
<b>Title:</b> Retrospective Study of the Loss of Heterozygosity at the p53, RB, DCC, and APC Tumor Suppressor Gene Loci in Patients with Multiple Primary Genitourinary (GU) Malignancies		
<b>Principal Investigator:</b> CPT Leah P. McMann, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Raymond S. Lance, MC; Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC; CPT Jeffrey A. Vos, MC; LTC Jerome B. Myers, MC		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Nov 00	<b>Periodic Review:</b> N/A

**Study Objective:** To investigate the roles and possible interactions of the tumor suppressor genes p53, RB, DCC, and APC in patients with multiple primary genitourinary (GU) malignancies.

**Technical Approach:** Using archival formalin-fixed, paraffin-embedded tumor specimens from patients from the MAMC Tumor Registry and from charts of patients identified and treated in the MAMC Urology Clinic, the plan is to look for LOH at the p53, RB, DCC and APC gene loci using restriction fragment length polymorphism (RFLP) analysis based on the polymerase chain reaction (PCR). DNA will be extracted from normal and tumor tissue and from deparaffinized tissue slides using the Puregene DNA Isolation Kit. PCR will be carried out using a DNA thermal cycler using 50 to 300 nG genomic DNA, 20 pMol of each primer, 75 mM of each dNTP, and 2 units of Taq DNA polymerase. PCR products will be digested overnight with 2 to 20 units of the appropriate restriction enzyme and run on an agarose or polyacrylamide gel which will be stained with ethidium bromide or SYBR green I and photographed under UV light.

**Progress:** 16 samples have been analyzed in FY00. Data collection continues. Protocol methods are being revised to utilize immunohistochemistry.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/005

**Status:** Ongoing

**Title:** Postpartum Durabilities of Anti-incontinent Surgery in Women of Childbearing Age

**Principal Investigator:** CPT Andrew C. Peterson, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** MAJ Sunil K. Ahuja, MC; LTC Robert C. Allen, Jr., MC; COL Gary D. Davis, MC; MAJ Patrick J. Woodman, MC; CPT Vanessa D. Dance, MC; CPT Mark Anderson, MC

**Start Date:**  
10/26/1999

**Est. Completion Date:**  
Aug 99

**Periodic Review:**  
N/A

**Study Objective:** To determine the rate of incontinence surgeries that are performed on women of childbearing age at Madigan Army Medical Center and the outcomes of bladder suspension/anti-incontinence surgeries in patients of childbearing age after vaginal or Caesarian section delivery.

**Technical Approach:** Charts will be reviewed on patients who have undergone anti-incontinent surgery at MAMC. Those patients of childbearing age (18-45) will be contacted by telephone and a questionnaire administered by the principal investigator. Results of the outcomes of the anti-incontinent surgery in those patients who have subsequently become pregnant and delivered a child will be analyzed. All patients who had become pregnant will be included in the study regardless of the method of delivery, Caesarian section versus vaginal delivery.

**Progress:** Four subject charts were review in FY00. Chart review continues.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/064	<b>Status:</b> Completed
<b>Title:</b> The Incidence of Testicular Microlithiasis in an Asymptomatic Screening Population		
<b>Principal Investigator:</b> CPT Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Raymond A. Costabile, MC; CPT Leah P. McMann, MC		
<b>Start Date:</b> 4/25/2000	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> N/A

**Study Objective:** (1) Establish the prevalence of microlithiasis in an asymptomatic population at risk for testicular cancer and (2) To correlate the prevalence of testicular microlithiasis with physical exam and other anatomical findings on scrotal ultrasound.

**Technical Approach:** Scrotal ultrasounds will be performed on males aged between 18 and 35 years who are undergoing physical examination as part of entrance into the year 2000 ROTC advanced camp and who volunteer to be a part of this study. A directed genitourinary history and physical will be conducted at the time of the ultrasound to establish the prevalence of testicular microlithiasis in an asymptomatic population.

**Progress:** This study enrolled 1504 subjects and found the incidence of testicular microlithiasis to be 5.8%. An abstract will be submitted as soon as the statistics are reviewed by a statistician.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/060

**Status:** Ongoing

**Title:** The Effect of 1,25-dihydroxyvitamin D3 (vitamin D) on Vascular Endothelial Growth Factor (VEGF) mRNA and Protein Expression in Prostate and Bladder Cancer Cell Lines

**Principal Investigator:** CPT Thomas L. Poulton, MC

**Department:** Surgery/Urology

**Facility:** MAMC

**Associate Investigator(s):** Lisa M. Pierce, D.Sc.; LTC Raymond A. Costabile, MC

**Start Date:**  
4/25/2000

**Est. Completion Date:**  
Apr 01

**Periodic Review:**  
N/A

**Study Objective:** To determine the effect of varying concentrations of 1,25-dihydroxyvitaminD3 (Vitamin D) on the expression of vascular endothelial growth factor (VEGF) mRNA and protein in prostate and bladder cancer cell lines in vitro. In addition, we will determine the effect of vitamin D exposure on telomerase activity in these prostate and bladder cancer cell lines.

**Technical Approach:** Cell Culture: The human prostate cancer cell line LNCaP and M12 and the human bladder cancer cell line T24 will be used for analysis in this study. After the cells reach confluency in their appropriate medias, the media will be replaced with fresh media containing either vehicle (0.1% ethanol) or various concentrations of 1,25-dihydroxyvitamin D3 for various times. The cells then will be processed for RNA extraction/Northern Analysis and for protein extraction/Western Analysis. The cells will also be extracted for telomerase activity

**Northern Analysis:** After total RNA extraction, the RNA will be resoved on a 0.8% agarose-formaldehyde gel, transferred to a Nytran filter and UV cross-linked to the membrane. After prehybridization, hybridization with probes of complementary DNAs for VEGF and 18S RNA will be carried out. Labeling will involve the use of alpha 32P dCTP and measurement is involve densitometry relative to VEGF mRNA present in the samples

**Western Analysis:** 30 uG of total protein lysates will be denatured and boiled prior to loading on a 12% polyacrylamide gell with a 5% stacking gel and transferred overnight onto a polyvinylidene difluoride membrane. After blocking, the membrane will be probed using a rabbit polyclonal anti-human VEGF antibody, and probed again with a mouse anti-glyceraldehyde-3phosphate dehydrogenase (GAPDH) antibody. The secondary will be a peroxidase-conjugated anti-mouse IgG antibody. Detection will be determined by densitometry using chemiluminescence

**Telomerase Activity:** Telomerase acitvey will be measured on prostate and bladder cancer cell lines using a commercially available kit (Telomerase PCR ELISA) following manufactureres (Boehringer Mannheim) instructions.

**Progress:** Two prostate cancer cell lines (LNCaP, M12) and a bladder cancer cell line (T24) were grown to confluency, serum starved for 48 hours, and exposed to various concentrations of 1,25 dihydroxyvitamin D3 (0, 10, 100 nM). At 2 days and 3 days of vitamin D exposure, supernatants were collected and cells were harvested and counted. VEGF secreted into the media was measured by enzyme linked immunosorbent assay. Telomerase activity was measured in the cells using the Telomerase Repeat Amplification Protocol. Results: All three cell lines secreted VEGF protein into the media, although M12 cells produced less VEGF than LNCaP cells ( $p < 0.05$ ; student t test) and T24 cells ( $p < 0.05$  student t test). In vitro vitamin D exposure did not reduce VEGF production in any of the prostate or bladder cancer cell lines. In addition, vitamin D did not decrease telomerase activity in any cell line. Conclusions: The anticarcinogenic effects of vitamin D do not appear to include downregulation of VEGF protein expression and telomerase activity in prostate and bladder cancer.

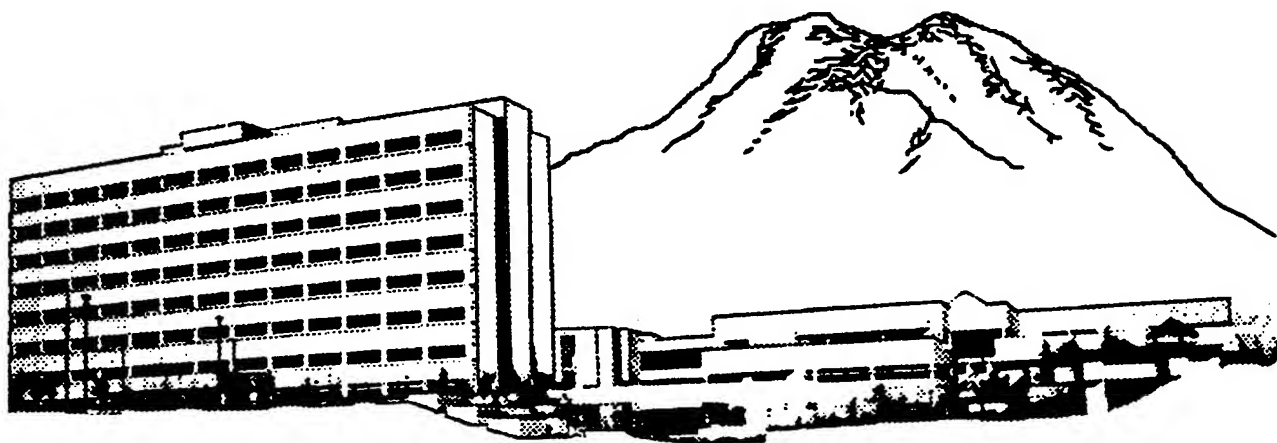
### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 96/158	<b>Status:</b> Ongoing
<b>Title:</b> Multi-center Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor Inflatable Penile Prosthesis		
<b>Principal Investigator:</b> MAJ Henry E. Ruiz, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ J. Brantley Thrasher, MC; CPT Douglas W. Soderdahl, MC; MAJ John B. Ellsworth, MC; MAJ Sunil K. Ahuja, MC; MAJ Raymond S. Lance, MC		
<b>Start Date:</b> 8/16/1996	<b>Est. Completion Date:</b> Oct 02	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** The primary effectiveness objective is to evaluate the ability of the AMS Ambicor inflatable penile prosthesis to provide an erection suitable for sexual intercourse (device function) as determined by physical examination and patient self-report. Secondary effectiveness objectives include estimating the effects of the prosthesis on patient sexual function and satisfaction, self-esteem, quality of life, and psychological well-being. The study will also evaluate levels of patient satisfaction with various aspects of the prosthesis including rigidity, length, girth and flaccidity. Safety will be evaluated by measuring rates of post implant complications (including device malfunction) and the occurrence of medical conditions.

**Technical Approach:** This is a multi-center, prospective, cohort study with the pre-implant experience of patients serving as the comparison for the evaluation of effectiveness and safety. The study sample will be derived from patients who present to the clinic with the diagnosis of erectile dysfunction. After an eligible patient makes an informed decision to be implanted with an AMS Ambicor penile prosthesis and signs the surgical consent he will be asked to participate in the study. A total of 250 patients will be recruited nationwide (12-20 being from MAMC) and will be implanted with the Ambicor inflatable penile prosthesis. The primary measure of effectiveness (sexual function, self-esteem, and psychological well-being), will be monitored for 2 years with visits at 6 weeks post-surgery, 6 months, 1 year, 18 months and 2 years. Follow-up for complications, associated medical conditions and other adverse device effects will be followed for 5 years with phone contact at 3 and 4 years, and a visit at 5 years.

**Progress:** Four patients enrolled in FY00, for a total of 29 patients. All SAEs have been reported to the IRB. Per the FDA, follow-up will continue through 18 months, decreased from 5 years.



## Detail Summary Sheets

Vascular Surgery,  
Department of Surgery

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/097

**Status:** Terminated

**Title:** Abdominal Aortic Aneurysm (AAA) and Chronic Obstructive Pulmonary Disease (COPD); Is There a Relationship

**Principal Investigator:** CPT Chatt A. Johnson

**Department:** Surgery/Vascular Surgery

**Facility:** MAMC

**Associate Investigator(s):** CPT Peter J. Armstrong, MC; LTC William H. Cragun, MC; COL Charles A. Andersen, MC; COL Thomas A. Dillard, MC; LTC Stephen B. Olsen, MC; COL David F. J. Tollefson, MC; CPT Eric A. Shry, MC

**Start Date:**  
4/21/1995

**Est. Completion Date:**  
Mar 96

**Periodic Review:**  
9/28/1999

**Study Objective:** To determine the association, if any, of AAA and COPD as well as potential pathophysiologic explanation.

**Technical Approach:** A comparison will be made between patients with and without COPD and the incidence of AAA. Patients 50 years and older will be selected from those followed in the pulmonary, family practice or adult primary care clinics who have been determined to have COPD by screening history, spirometry and carbon monoxide diffusing capacity (DLCO). Controls will be age/sex matched without COPD. Selected participants will be evaluated by pulmonary function tests (spirometry, DLCO), serum alpha 1 anti-trypsin levels, serum elastase levels, serum cholesterol levels, ankle-brachial indices and abdominal aortic duplex. The incidence in the control and study groups will be compared through Chi-squared analysis and individual variables will be determined through student T-test. A  $p < 0.05$  will be determined to be statistically significant. Patients and primary care physicians will be notified of the presence or absence of AAA, abnormal ankle-brachial indices, COPD, or hypercholesterolemia.

**Progress:** This protocol was terminated by the PI, 27 Jun 00, due to the PCS of its original PI and lack of staff and time to work on the project.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/098

**Status:** Ongoing

**Title:** A Multicenter, Double-blind, Randomized, Parallel Placebo-Controlled Study of the Safety and Efficacy of Chronic Oral Beraprost Sodium in Patients with Intermittent Claudication (Fontaine Stage II Peripheral Arterial Occlusive Disease)

**Principal Investigator:** COL David F. J. Tollefson, MC

**Department:** Surgery/Vascular Surgery

**Facility:** MAMC

**Associate Investigator(s):** COL Charles A. Andersen, MC; LTC Stephen B. Olsen, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 02

**Periodic Review:**  
N/A

**Study Objective:** Primary objective of this study is evaluation of Beraprost Sodium (BPS) on exercise capacity as assessed by a defined treadmill walk test in patients with intermittent claudication (Fontaine Stage II peripheral arterial occlusive disease, (PAOD). Absolute claudication distance (ACD) will be the primary efficacy endpoint. Secondary objectives: (1) Evaluation of the effect of Beraprost Sodium on Initial Claudication Distance, (2) Evaluation of the safety of BPS in these patients, assessed by adverse events and clinical laboratory parameters, (3) Evaluation of the effect of BPS on the quality of life assessments, and (4) Evaluation of the effect of BPS on the percentage of responders to drug treatment.

**Technical Approach:** This study will evaluate up to 12 subjects at MAMC for intermittent claudication. After an initial screening exam including physical, neurological, cardiovascular, and cutaneous exams, the subjects will be started on a single-blind (patient blinded) placebo run-in period. During this time, the patient will be monitored to see if they improve significantly without the use of actual medication. Additionally, they will be checked to make sure that they are taking their medication in a timely manner. Subjects who take their medication regularly and who do not exhibit too much improvement in the first 3-week period will then be started on a double-blind, placebo controlled study period of 48 weeks. Subjects will periodically be seen for physical exams and administered treadmill tests. Results of subject treadmill tests and QOL questionnaires will be used to assess objective outcomes.

**Progress:** 29 patients have been enrolled in this study in FY00 at MAMC. Nine patients were screen failures. 20 patients have been randomized, with 19 patients completing the treatment period and 1 withdrawal due to an adverse event (not of a serious nature). Eleven patients have completed the study with 9 patients continuing to be followed. All SAEs have been reported to the IRB. Patient enrollment continues.

### Detail Summary Sheet

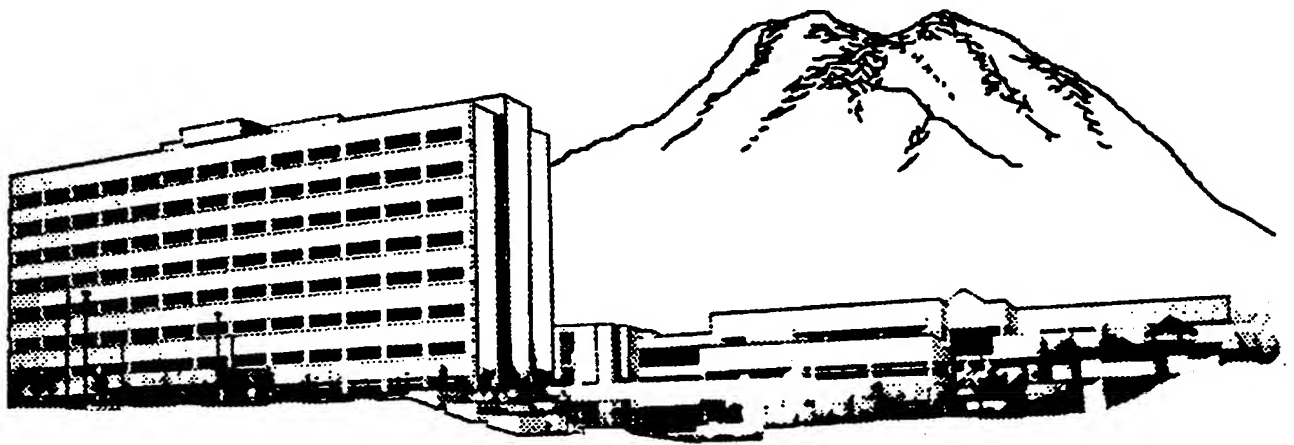
<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/081	<b>Status:</b> Ongoing
<b>Title:</b> A Double-Blind, Randomized, Parallel Group, Placebo-Controlled Study to Evaluate the Safety and Efficacy of NM-702 in Subjects with Intermittent Claudication		
<b>Principal Investigator:</b> COL David F. J. Tollefson, MC		
<b>Department:</b> Surgery/Vascular Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Stephen B. Olsen, MC; COL Charles A. Andersen, MC; CPT Chatt A. Johnson		
<b>Start Date:</b> 7/27/1999	<b>Est. Completion Date:</b> Aug 00	<b>Periodic Review:</b> 7/27/2000

**Study Objective:** (1) Demonstrate the efficacy of NM-702 at three different doses compared to placebo in the treatment of patients with intermittent claudication. The following assessments will be used to determine efficacy: improvement in peak walking time, improvement in claudication onset time, and change in functional status as measured by the Health Status Survey Questionnaire and Walking Impairment Questionnaire, (2) Assess the safety of NM-702 treatment in subject population as determined by physical examination, blood and urine analysis, Holter monitoring, 12-lead. ECG, blood pressure measurements and by evaluation of adverse events and concomitant medication usage.

**Technical Approach:** This will be a double-blind, parallel-group, dose- response study in which subjects will be randomized to receive either 1, 2, or 4 mg of NM-702, or placebo, twice a day for 12 consecutive weeks. A total of 200 evaluable subjects (50 per group) will be studied. A minimum of 10 study sites will participate in this trial. Total study time per subject, including follow-up, is one year.

Subjects will be seen in clinic 2-3 times during the screening period to obtain two consecutive treadmill results (peak walking time) that are within 25% of each other on separate days. Also, ail baseline information will be collected on the first screen attempt. Upon enrollment into the study, subjects will be required to walk on the treadmill until claudication onset, administered two assessment questionnaires and given drug. Subjects will return to clinic for three visits over the ensuing 12 week treatment period. At that time, EKGS, treadmill test for claudication onset time, and assessment questionnaires will be performed. Subjects will be seen twice in clinic during follow-up period. Adverse events, including significant laboratory abnormalities, will be recorded on the Case Report Forms.

**Progress:** 16 patients have been enrolled in this study in FY 00 at MAMC, with 4 patients screen failures. 12 patients have been randomized to study drug and will be followed until September 2002. All adverse events have been reported to the IRB. Patient enrollment continues.



## Detail Summary Sheets

Weed Army Community Hospital

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/084	<b>Status:</b> Completed
<b>Title:</b> Confirmation of Endotracheal Tube Placement by Special Operations Combat Corpsmen and Medics		
<b>Principal Investigator:</b> MAJ Charles Price, AN		
<b>Department:</b> WACH	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Mark D. Calkins, MC		
<b>Start Date:</b> 6/19/1998	<b>Est. Completion Date:</b> Jul 99	<b>Periodic Review:</b> 7/27/1999

**Study Objective:** To evaluate the effectiveness of several techniques in determining endotracheal tube placement when used by combat corpsmen and medics.

**Technical Approach:** The trachea and esophagus will be intubated with an identical tube. Randomization will determine which ETT will be checked (either the tracheally or esophageally placed ETT) and the order which each technique will be used to determine whether the ETT is in the esophagus or trachea. Techniques used will include observation only with ventilation of randomized ETT, stethoscope, esophageal detector device, colorimetric end-tidal CO2 detector, stethoscope and EDD and stethoscope and ETCO2. The medic will be allowed up to 6 breaths via an adult ambu bag and not to exceed 30 seconds to assess proper ETT placement. They will then leave the operating room and report their findings on an assessment form. Three evaluations per patient are likely, but dependent on the clinical/surgical situation.

**Progress:** Ten subjects were enrolled in this study with no adverse events noted during study participation. The effectiveness of the six techniques evaluated in determining endotracheal tube placement were the following:

Observation, 12/14 correct (85.7% success rate)

Stethoscope, 11/14 correct (78.5% success rate)

ETCO2 detector, 13/14 correct (92.8% success rate)

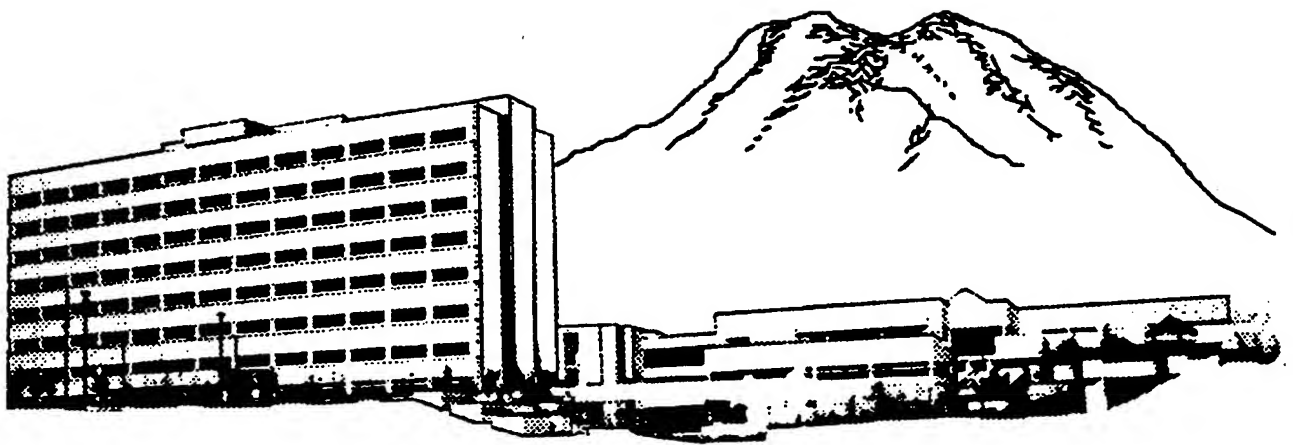
Esophageal detector device (EDD), 14/14 correct (100% success rate)

Steth/EDD, 14/14 correct (100% success rate)

Steth/ETCO2, 14/14 correct (100% success rate)

The incorrect evaluations were performed by the most experienced medics\*\*, (>6yrs experience with advanced training) and the stethoscope alone method was the least effective. The most effective techniques were the combination evaluations and the EDD alone. The EDD was not only 100% effective but was the most quickly determined evaluation (always within the first attempt). The full six ventilations were used with the least effective evaluation methods. Further study should include evaluation of the EDD and ETCO2 detectors with common battlefield injuries (open chest wounds) and a larger number evaluation with out of hospital intubations using EMT's

\*\* Experience Levels <3yrs (n=2), 3-6 yrs (n=1), and >6yrs (n=7)



## **Detail Summary Sheets**

Gynecology Oncology Group

### Detail Summary Sheet

Date: 29 Sep 00	Number: 81/035	Status: Ongoing
Title: GOG 0041: Surgical Staging of Ovarian Carcinoma		
Principal Investigator: COL Mark E. Potter, MC		
Department: GOG	Facility: MAMC	
Associate Investigator(s): COL Roger B. Lee, MC; COL William L. Benson, MC		
Start Date: 1/16/1981	Est. Completion Date: Jan 86	Periodic Review: 10/5/2000

**Study Objective:** To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

**Technical Approach:** This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a completed and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

**Progress:** This study was closed to patient entry, 12 Feb 87. Thirteen patients were enrolled. Eight patients remain disease free at least 12 years after therapy and continued to be followed at MAMC during FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 81/105

**Status:** Ongoing

**Title:** GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG

**Facility:** MAMC

**Associate Investigator(s):** COL William L. Benson, MC; COL Roger B. Lee, MC; LTC Gordon O. Downey, MC

**Start Date:**  
8/21/1981

**Est. Completion Date:**  
Mar 98

**Periodic Review:**  
10/5/2000

**Study Objective:** To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG 0025.

**Technical Approach:** Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

**Progress:** This study was closed to patient entry, 20 Jul 85. Six patients were enrolled. One patient, is disease free 18 years after completing therapy, and continued to be followed at MAMC during FY 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 84/033	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease		
<b>Principal Investigator:</b> COL Mark E. Potter, MC		
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Roger B. Lee, MC; COL William L. Benson, MC		
<b>Start Date:</b> 2/17/1984	<b>Est. Completion Date:</b> Dec 88	<b>Periodic Review:</b> 10/5/2000

**Study Objective:** To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

**Technical Approach:** Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for five years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

**Progress:** This study was closed to patient entry 25 Feb 92. Ten patients were enrolled; of these, one patient died and 9 patients continue to be followed.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 84/074

**Status:** Ongoing

**Title:** GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG

**Facility:** MAMC

**Associate Investigator(s):** COL Roger B. Lee, MC; COL William L. Benson, MC

**Start Date:**  
8/17/1984

**Est. Completion Date:**  
Jul 89

**Periodic Review:**  
10/5/2000

**Study Objective:** To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

**Technical Approach:** Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** This study was closed to patient entry, 10 Feb 92. One patient continued to be followed at MAMC during FY 00 and remains disease-free off-therapy.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 86/089      **Status:** Ongoing

**Title:** GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG      **Facility:** MAMC

**Associate Investigator(s):** COL William L. Benson, MC; COL Roger B. Lee, MC; LTC Gordon O. Downey, MC

**Start Date:**  
8/15/1986

**Est. Completion Date:**  
Feb 94

**Periodic Review:**  
10/5/2000

**Study Objective:** To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

**Technical Approach:** Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

**Progress:** This study was closed to patient entry, 3 Dec 90. Two patients, disease free ten years after completion of therapy, continued to be followed at MAMC during FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 87/104

**Status:** Ongoing

**Title:** GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG

**Facility:** MAMC

**Associate Investigator(s):** COL Roger B. Lee, MC; COL William L. Benson, MC; COL Donald H. Kull, MC

**Start Date:**  
8/21/1987

**Est. Completion Date:**  
Indef

**Periodic Review:**  
10/5/2000

**Study Objective:** To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

**Technical Approach:** All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

**Progress:** This study was closed to patient entry, 18 Dec 95. One patient, enrolled in FY 88, remains disease free and continued to be followed at MAMC during FY 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 87/028	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III		
<b>Principal Investigator:</b> COL Mark E. Potter, MC		
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Roger B. Lee, MC; COL William L. Benson, MC		
<b>Start Date:</b> 11/21/1986	<b>Est. Completion Date:</b> Indef	<b>Periodic Review:</b> 10/5/2000

**Study Objective:** In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAi and IBi patients with poorly differentiated tumors and stage IAii and IBii (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

**Technical Approach:** The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin in patients with ovarian cancer. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m<sup>2</sup> IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** This study was closed to patient entry, 14 Mar 94. Five patients were enrolled. One patient, who remains disease free, continued to be followed at MAMC during FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 87/091

**Status:** Ongoing

**Title:** GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG

**Facility:** MAMC

**Associate Investigator(s):** COL Roger B. Lee, MC; COL William L. Benson, MC

**Start Date:**  
6/19/1987

**Est. Completion Date:**  
Indef

**Periodic Review:**  
10/5/2000

**Study Objective:** To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

**Technical Approach:** Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGy in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

**Progress:** This study was closed to patient entry, 3 Jul 95. Three patients were enrolled. All are currently clinically disease free and continue to be followed during FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 91/086                      **Status:** Ongoing

**Title:** GOG 0109 (SWOG 8797): A Randomized Comparison of 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy, versus Radiation Therapy Alone in Selected Patients with Stages I-A2, I-B, and II-A Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG    **Facility:** MAMC

**Associate Investigator(s):** None.

**Start Date:**  
8/2/1991

**Est. Completion Date:**  
Sep 94

**Periodic Review:**  
10/5/2000

**Study Objective:** To determine whether the combination of 5-fluorouracil (5-FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins following radical hysterectomy and lymph node dissection for Stages I-A2, I-B, and II-A carcinoma of the cervix and to determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

**Technical Approach:** Patients must have primary, histologically confirmed, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix, clinical stages I-A2, I-B, or II-A and must have had a radical hysterectomy with total pelvic lymphadenectomy and para-aortic sampling. Patients must have, at surgical evaluation, either histologically confirmed positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins. Patients with confirmed positive para-aortic lymph nodes are not eligible. Patients must not have received prior chemotherapy, immunotherapy (including biologics), hormonal therapy, or pelvic irradiation. Patients will be randomly assigned to receive either 5-FU and cisplatin plus pelvic irradiation or pelvic irradiation alone. Patients with positive high common iliac lymph nodes will receive extended field para-aortic irradiation. Irradiation and chemotherapy will begin simultaneously within six weeks after surgery. Chemotherapy will be given once a week every three weeks for four cycles. Radiation therapy will be given for six weeks. After completion of therapy, patients will be followed every 3 months for two years and every 6 months thereafter. Formal analysis of progression-free and overall survival will be performed at 2 1/2 years after the start of patient accrual to determine if consideration should be given to early termination of either treatment arm.

**Progress:** This study was closed to patient entry, 20 May 94. One patient, enrolled in 1991, remains without evidence of recurrence of disease and continued to be followed during FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 91/074

**Status:** Ongoing

**Title:** GOG 0115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, and Unclassified Sex Cord Stromal Tumor)

**Principal Investigator:** COL Mark E. Potter, MC

**Department:** GOG

**Facility:** MAMC

**Associate Investigator(s):** None.

**Start Date:**  
7/12/1991

**Est. Completion Date:**  
Indef

**Periodic Review:**  
10/5/2000

**Study Objective:** To assess the efficacy of bleomycin, etoposide (VP-16), and cisplatin (BEP) chemotherapy in patients with malignant tumors of the ovarian stroma as a first-line regimen.

**Technical Approach:** Eligible patients will be those with histologically confirmed primary Stages II, III, or IV with incompletely resected disease, recurrent or persistent tumor of the ovarian stroma (granulosa cell tumor, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord stromal tumor, or sex cord tumor with annular tubules). Patients will undergo, where appropriate, a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Omentectomy, cytologic washings, and other surgical staging such as pelvic and peri-aortic node sampling, multiple pelvic and diaphragmatic node biopsies are optional. Within 8 weeks of surgery, patients will be placed on BEP therapy: bleomycin IV push weekly for nine weeks, etoposide IV daily times five every three weeks for four courses, cisplatin IV daily times five, every three weeks for four courses. Complete responders or patients with nonmeasurable disease will undergo reassessment laparotomy not later than eight weeks following final course of therapy. To be evaluable for response, a patient will receive at least one course of chemotherapy. The efficacy of the three-drug combination will be evaluated by frequency of negative second-look and frequency and severity of acute toxicity.

**Progress:** This study was closed to patient entry, April 1997. One patient had disease detected at second look laparotomy in Sep 98. However, she still has no clinical evidence of disease and continued to be followed during FY 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 93/063	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix		
<b>Principal Investigator:</b> COL Mark E. Potter, MC		
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start Date:</b> 3/5/1993	<b>Est. Completion Date:</b> Oct 97	<b>Periodic Review:</b> 10/5/2000

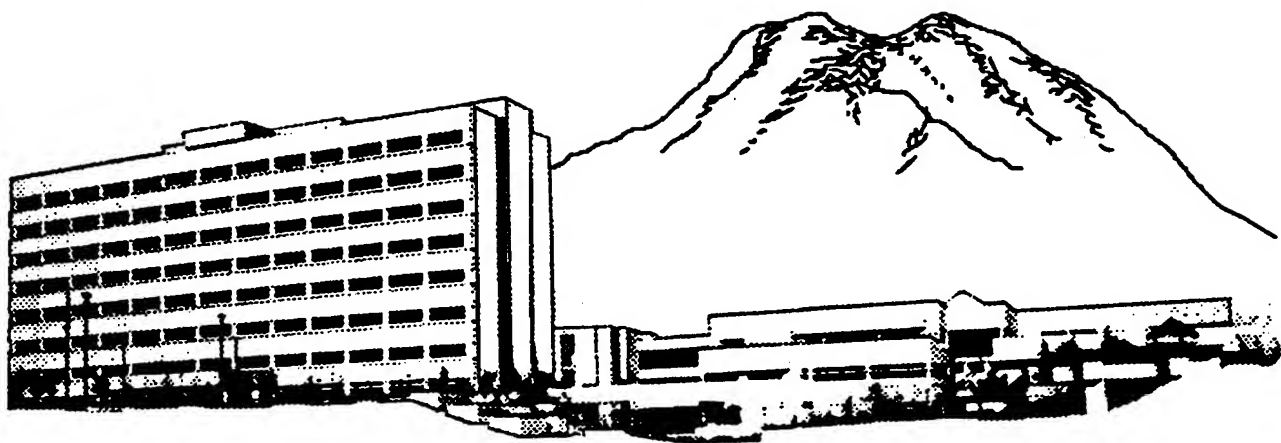
**Study Objective:** To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.

**Technical Approach:** This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m<sup>2</sup> not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens

The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered.

**Progress:** This study was closed to patient entry, April 1997. One patient was enrolled who remains without evidence of recurrence of disease and continued to be followed at MAMC during FY 00.





## **Detail Summary Sheets**

National Surgical Adjuvant Breast & Bowel Project

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/001	<b>Status:</b> Ongoing
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**Title:** NSABBP C-06: A Clinical Trial Comparing Oral Uracil/Ftorafur (UFT) Plus Leucovorin (LV) with 5-Fluorouracil (5-FU) Plus LV in the Treatment of Patients with Stages II and III Carcinoma of the Colon

**Principal Investigator:** MAJ David E. McCune, MC

<b>Department:</b> NSABBP	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Matthew P. Jones, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
10/20/1998

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
10/26/1999

**Study Objective:** (1) To compare the relative efficacy of UFT + LV with that of 5-FU + LV in prolonging DFS and S, (2) to evaluate the prognostic significance of the proposed biomarkers, alone or in combination, in patients treated with 5-FU + LV or UFT + LV, (3) to evaluate relationships of various biomarkers to each other and to evaluate their association with patient and tumor characteristics, (4) to compare QOL in patients with stage II or III carcinoma of the colon treated with either the 5-FU + LV regimen or the UFT + LV regimen.

**Technical Approach:** Patients will be randomized to one of two chemotherapy regimens following resection of stage II and III carcinoma of the colon. Group 1 will receive 5-Fluorouracil plus high-dose Leucovorin and Group 2 will receive Uracil/Ftorafur plus Leucovorin. Patients will be stratified according to the number of positive nodes.

**Progress:** This protocol was closed to patient accrual 31 Mar 99. One patient was enrolled in FY 99 at MAMC and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/147

**Status:** Ongoing

**Title:** NSABBP R-03: A Clinical Trial to Evaluate the Worth of Preoperative Multimodality Therapy (5-FU-LV and RTX) in Patients with Operable Carcinoma of the Rectum

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** NSABBP

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ John R. Caton, MC; MAJ Richard F. Williams, MC

**Start Date:**  
8/6/1993

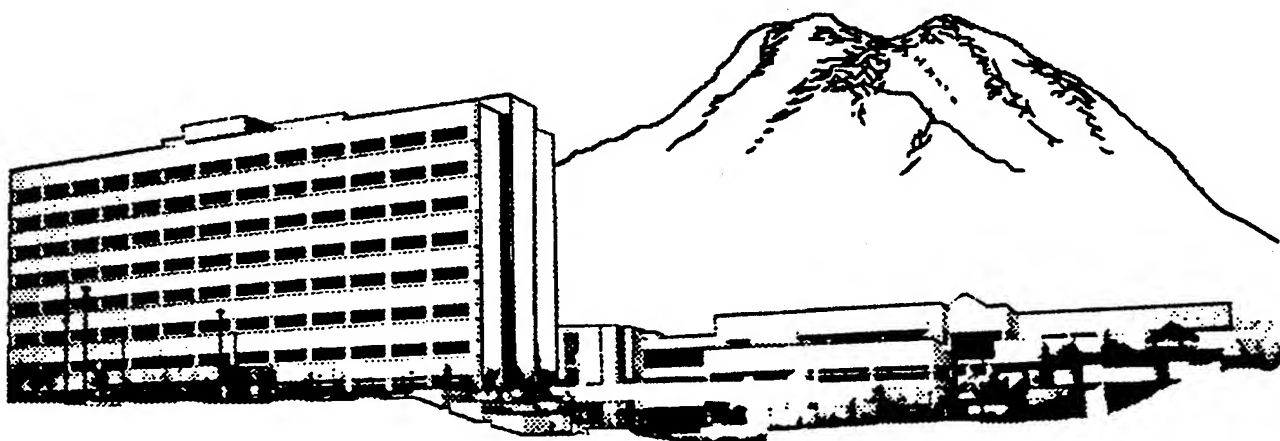
**Est. Completion Date:**  
Jul 98

**Periodic Review:**  
8/1/1999

**Study Objective:** 1). To determine whether the administration of chemotherapy (chemo) with radiotherapy (RTX) preoperatively is more effective than administration of chemo and RTX (C&R) postoperatively in improving disease-free survival and survival in patients with operable carcinoma of the rectum. 2). To determine if the administration of the above C&R preoperatively results in improvement local recurrence rates when compared with the regimen administered post-operatively in this population of patients. 3). To evaluate the response of rectal tumors to preoperative C&R and to correlate that response with disease-free survival and survival. 4). To assess the downstaging effect of preoperative C&R on the tumor size and pathologic status of regional lymph nodes. 5). To estimate the proportion of patients who can be converted to sphincter-saving surgical procedures from abdomino-perineal resection and local excision alone.

**Technical Approach:** Patients with operable adenocarcinoma of the rectum will receive seven cycles of 5-FU (FU) + leucovorin (LV) and radiotherapy (RTX), where the first three cycles are given preoperatively and the remaining four postoperatively, to seven cycles of FU-LV and RTX given postoperatively. The patients will be randomized into 2 groups. Group 1 patients, in cycle 1, will receive LV 500 mg/m<sup>2</sup> by IV infusion and FU 500 mg/m<sup>2</sup> will be started 1 hr later. Treatment will be given weekly for 6 weeks followed by a rest period. Treatment will be restarted 21 days after the date of administration of the sixth dose of the previous cycle. RTX will begin after completion of cycle 1. FU 325 mg/m<sup>2</sup>/day and LV 20 mg/m<sup>2</sup>/day will be given for 5 days during the first and fifth weeks of RTX (cycles 2 and 3). Surgery will be performed after completion of radiation therapy. After recovery from surgery, four more cycles of FU with LV, as in cycle 1, will be given for a total of seven cycles. Groups 2 patients should have surgery performed no later than 3 weeks after randomization. Chemo will begin after recovery from surgery is complete but no later than 4 weeks postoperatively. LV and FU will be administered as in Group 1. RTX will begin after completion of cycle 1. Cycle 4 should begin after completion of RTX when counts allow, but no later than 5 weeks. Four more cycles of FU with LV will be given for a total of seven cycles.

**Progress:** This protocol was closed to patient accrual 27 Aug 99. One patient was enrolled at MAMC and continues to be followed.



## Detail Summary Sheets

### Pediatric Oncology Group

### Detail Summary Sheet

Date: 29 Sep 00

Number: 98/073

Status: Ongoing

Title: POG 8602: Evaluation of Treatment Regimens in Acute Lymphoid Leukemia of Childhood (ALinC #14)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: POG

Facility: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

Start Date:  
5/22/1998

Est. Completion Date:  
Pend

Periodic Review:  
5/23/2000

**Study Objective:** (1) To test the concept that intensive asparaginase (ASP) therapy, designed to maintain low asparagine levels for the first six months of maintenance will improve the outcome for patients with standard risk acute lymphocytic leukemia (ALL) when added to pulses of intermediate dose methotrexate (IDM), as compared to intensification with IDM alone, (2) to study the effectiveness in standard risk patients of intensification with a potentially synergistic or additive drug pair, i.e., IDM plus arabinosyl cytosine (AraC), as compared to that of intensification with IDM pulses alone, (3) to determine if administering a pulse of IDM + AraC at three week intervals (early intensification) during the first 4 months of complete remission in children with ALL is superior to administering the same number of IDM + AraC pulses at 12 week intervals (late intensification) during the first two years of complete remission in children with ALL with either "lower" or "higher" risk of relapse, (4) to obtain further information on the immediate and delayed toxicity of the continuation chemotherapy program that incorporates these combinations of methotrexate (MTX) and AraC or MTX and ASP in moderately high doses, (5) to continue to characterize the biological features of acute lymphatic leukemia of childhood, and their independence and interaction (with therapy and each other) as prognostic factors for attaining and maintaining remission, (a) To assess the effectiveness of these regimens for the early pre-B (non-T, non-B, non-pre-B) and pre-B immunophenotypes of All, respectively, (b) To investigate the hypothesis that ploidy and/or the presence of structural chromosome abnormalities predicts prognosis, (6) to learn whether outcome is related to individual patient differences in methotrexate (MTX) availability as measured by sequential determinations of red blood cell (RBC) MTX and folate levels.

**Technical Approach:** This study has been closed to patient accrual; however HHS guidelines has required IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 3 patients being followed who were consented on IRB approved 8823 studies in other POG institutions. Follow-up information on these patients will need to be sent to the POG Statistical Office per protocol requirements.

**Progress:** Protocol is closed to patient accrual; however 2 patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/076

**Status:** Ongoing

**Title:** POG 8615: A Phase III Study of Large Cell Lymphomas in Children and Adolescents: A Comparison of Two Treatment Regimens - ACOP+ versus APO

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
5/22/1998

**Est. Completion Date:**  
Indef

**Periodic Review:**  
5/23/2000

**Study Objective:** (1) To determine the influence of alkylating agent (cyclophosphamide) therapy in advanced-stage large cell lymphomas in children and adolescents, by comparing in a randomized prospective study the efficacy and toxicity of a modified ACOP+ versus a modified APO regimen, (2) to reduce the adverse effects of treatments by elimination of involved field and cranial radiation in the treatment of large cell lymphomas, (3) to evaluate the adequacy of one year of total therapy for advanced large cell Non-Hodgkin's lymphoma (NHL), (4) to study clinical pathologic patterns and biologic characteristics of large cell lymphomas in children and adolescents, (5) to assess the feasibility of the total dose of Adriamycin of 300 mg/M2 on the APO arm (post closure of randomization).

**Technical Approach:** This study has been closed to patient accrual; however HHS guidelines has required IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 1 patient being followed who was consented on an IRB approved 8615 study at Stanford. Follow-up information on this patient will be sent to the POG Statistical Office per protocol requirements.

**Progress:** Protocol is closed to patient accrual; however 1 patient continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/141

**Status:** Ongoing

**Title:** POG 8650: Intergroup National Wilms' Tumor Study - 4

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
6/9/1993

**Est. Completion Date:**  
Oct 97

**Periodic Review:**  
5/23/2000

**Study Objective:** To compare (1) the relapse-free and overall survival percentages of patients with: Stage I and II favorable histology (FH) and Stage I anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with Vincristine and actinomycin D, (2) Stages 3 and 4 FH, and Stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I Vincristine, actinomycin D, and Adriamycin plus radiation therapy, (3) Stages 2-4 Ana treated with Vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy, and (4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

**Technical Approach:** All patients will be <16 years of age, have had no prior chemo-radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol. Patients will be randomized as follows: Stage II/FH & Stage I Ana receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D + C (65 wks) plus RT or A + V + D + C (65 wks) plus RT.

Legend: A = actinomycin D, V = Vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

**Progress:** This protocol was closed to patient entry, 1 Sep 94. One patient was enrolled at MAMC in FY 93 and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/074	<b>Status:</b> Ongoing
<b>Title:</b> POG 8823/34: Recombinant Alpha-Interferon in Childhood Chronic Myelogenous Leukemia		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 5/22/1998	<b>Est. Completion Date:</b> Pend	<b>Periodic Review:</b> 5/23/2000

**Study Objective:** (1) To determine toxicity, response rate and duration of response to therapy with recombinant alpha interferon for newly diagnosed "adult" chronic myelogenous leukemia (ACML) in chronic phase, and for "juvenile" chronic myelogenous leukemia (JCML) occurring within the first two decades. (2) to obtain prospective clinical, laboratory, and genetic data on cases of ACML and JCML treated with recombinant alpha interferon.

**Technical Approach:** This study has been closed to patient accrual; however HHS guidelines has required IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 3 patients being followed who were consented on IRB approved 8823 studies at Walter Reed Army Medical Center. Follow-up information on these patients will need to be sent to the POG Statistical Office per protocol requirements.

**Progress:** Protocol is closed to patient accrual; however 3 patients continue to be followed.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/075	<b>Status:</b> Ongoing
<b>Title:</b> POG 9005: ALinC #15 - Dose Intensification of Methotrexate and 6-Mercaptopurine for ALL in Childhood - A Randomized Phase III Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 5/22/1998	<b>Est. Completion Date:</b> Pend	<b>Periodic Review:</b> 5/23/2000

**Study Objective:** (1) To determine, in a randomized trial, whether intensification with intermediate-dose methotrexate (ID MTX), and intravenous 6-mercaptopurine (IV 6-MP) is superior or inferior to repeated low-dose, oral methotrexate (LD MTX) and IV 6-MP for prevention of relapse in children with ALL in first remission and at lower risk for relapse, (2) To compare, in a randomized trial, intensification with ID MTX alone versus ID MTX and IV 6-MP for prevention of relapse in children with lower risk ALL in first remission, (3) To determine if RBC MTX/folate levels can be correlated with event free survival.

**Technical Approach:** This study has been closed to patient accrual; however HHS guidelines has required IRB approval of closed studies when patients are being followed for survival information. Madigan currently has 5 patients being followed who were consented on IRB approved 9005 studies in other POG institutions, 4 military medical centers and two civilian. Follow-up information on these patients will need to be sent to the POG Statistical Office per protocol requirements.

**Progress:** Protocol is closed to patient accrual. 1 patient died and 5 patients continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/018	<b>Status:</b> Ongoing
<b>Title:</b> POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC		
<b>Start Date:</b> 11/18/1994	<b>Est. Completion Date:</b> Nov 94	<b>Periodic Review:</b> 5/23/2000

**Study Objective:** (1) To compare the 2-year event-free survival (EFS) of children with newly-diagnosed high-risk medulloblastoma who are treated with cisplatin and VP-16 pre-irradiation vs post-irradiation, (2) To define the toxicity and activity of pre-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma, (3) To determine whether achievement of a measurable tumor response (PR and CR) to pre-irradiation cisplatin/VP-16 has prognostic significance for children with high-risk medulloblastoma, compared with failure to achieve a measurable response (SD or PD), (4) To define the toxicity and activity of post-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma, and (5) To determine if c-myc amplification in medulloblastoma is associated with an adverse prognosis.

**Technical Approach:** Studies in children and adults have demonstrated the ability to deliver pre-radiotherapy chemotherapy for patients with newly-diagnosed brain tumors without increasing neurotoxicity in association with the subsequent radiotherapy. This approach creates a phase II "window" allowing evaluation of response in these patients who are previously untreated except for surgery. The theoretical anti-neoplastic advantage of this approach is the potentially enhanced efficacy of the radiotherapy when given to "chemically debulked" patients. Half of the children diagnosed with medulloblastoma are now being successfully treated and are surviving for prolonged periods. Until recently, the survival of this group of patients was limited so that long-term effects of therapy were not a concern. As survival increases, one would expect to observe an increase in frequency of certain treatment-related toxicities. There are now a variety of long-term effects which need to be considered in this cohort of patients. Specific evaluations will be made on all patients entered onto this study, so that treatment-related problems may be detected in their early stages and intervention taken. This approach should ultimately improve the quality of life for children diagnosed and treated for brain tumors.

**Progress:** This protocol closed to patient entry 26 Mar 96. One patient was enrolled in this study at MAMC in FY 95 and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/164

**Status:** Ongoing

**Title:** POG 9047: Neuroblastoma Biology Protocol

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; COL Bruce A. Cook, MC; COL Stephen R. Stephenson, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
9/3/1993

**Est. Completion Date:**  
Feb 96

**Periodic Review:**  
8/22/2000

**Study Objective:** (1) To obtain tissue for the analysis of DNA content of neuroblastoma cells by flow cytometry, (2) To characterize neuroblastoma tumor DNA from POG patients genetically by analysis of N-myc amplification and LOH for chromosome 1p, (3) To develop a reference bank of genetically characterized tumor tissue and DNA that would be available for other studies.

**Technical Approach:** This is a non-therapeutic study intended to collect tissue from newly-diagnosed neuroblastoma patients = 21 years. Viable tumor tissue, frozen tumor tissue (or marrow) and serum will be collected and forwarded to a designated study site.

**Progress:** No patients were enrolled in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 95/084	<b>Status:</b> Completed
<b>Title:</b> POG 9182: HIV/Malignancy Biology Protocol			
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC			
<b>Department:</b> POG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC			
<b>Start Date:</b> 3/17/1995	<b>Est. Completion Date:</b> Apr 97		<b>Periodic Review:</b> 2/22/2000

**Study Objective:** (1) To establish a national registry of pediatric AIDS-associated lymphomas and other malignancies and a repository of well-characterized tumor tissue, cells and sera from affected patients, (2) To conduct prospective Phase I-III clinical trials of anti-cancer and anti-retroviral therapies aimed at improving outcomes and identifying critical determinants of risk, (3) To identify the presence and quantify the viral burden of human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), Human Herpes virus 6 (HHV6), and Herpes Simplex virus (HSV) in the tumor tissue, peripheral blood cells, plasma, and cerebrospinal fluid of pediatric patients with lymphomas and other malignancies; and to characterize the effect of anti-cancer and antiviral chemotherapy with regard to lymphoma stage, disease progression, host response, and toxicity, (4) To conduct the first large-scale molecular epidemiologic study of risk factors related to development of HIV-related NHL in children by means of a case-control analysis of HIV-infection characteristics such as co-infection with EBV, CMV, HHV6, Mycoplasma, the quantitative host viral burden, level of immunodeficiency, and other host characteristics, and (5) For HIV+ and HIV- children, to characterize differences in NHL tumor tissue in terms of immunophenotype, immunoglobulin gene rearrangements and oncogene (c-myc) activation.

**Technical Approach:** Three groups of children are eligible for this protocol. The first, a "case" group, consists of children with a newly-diagnosed malignancy who are HIV positive. The second, a "malignancy control" group, consists of children with a newly-diagnosed malignancy who do NOT have HIV infection. The third group, a "non-malignancy control" group, consists of children with no evidence of malignancy, but who have a documented HIV infection. A total of 150, 150, and 300 patients, respectively is expected. The subject will be seen in the clinic at least every two months for up to two years, then every 6 months up to 3 years. At each visit blood will be drawn for testing. In addition, a small piece of tumor tissue or other body fluids (including spinal fluid and bone marrow), already obtained as part of routine clinical management may be examined. We will establish a database as a repository for characteristics of pediatric patients with HIV infection and malignancies. The database will include all appropriate clinical parameters, laboratory measures, and results of molecular and virologic studies. Descriptive analyses of clinical and laboratory data will use various criteria to characterize the study population and to correlate variation in infectious virus and total viral burden with clinical course and other laboratory measurements. Primary endpoints, which may include tumor response, disease-free survival and episodes of grade 3-4 toxicities, will be confined to those specified in POG therapeutic protocols. Contingency tables relating the laboratory variables with stage, age, primary tumor site, histopathology, and clinical response will be produced. Conditional logistic regression will be used to compare biological data for cases to matched controls. Frequency matching will be performed at the Statistics Office at the time of analysis. Kaplan-Meier life tables, log rank tests, and Cox regression will be used to explore the relationship of laboratory variables to outcome.

**Progress:** This study closed to further patient enrollment 22 Sep 00. No patients were enrolled in this protocol at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/056

**Status:** Ongoing

**Title:** POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
12/16/1994

**Est. Completion Date:**  
Dec 99

**Periodic Review:**  
5/23/2000

**Study Objective:** (1) To confirm the outstanding results in patients with lesser risk not-T, non-B acute lymphoblastic leukemia (ALL) treated in a fashion similar to the least intensive arm of POG 8602 (AlinC 14, Arm A), (2) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406.

**Technical Approach:** Patients on this study will be treated with a 3-drug induction regimen (Vincristine, prednisone, and L-asparaginase) to bring about remission (a state of no apparent disease) in four weeks

This will be followed by a consolidation phase including (6) six courses of intravenous (into vein) intermediate-dose methotrexate (each will require hospital stay) at 3-week intervals. After week 5, daily 6-mercaptopurine will be given by mouth until the end of planned treatment. Methotrexate will be given intramuscularly (into muscle) weekly. Periodic "pulses" (infrequent administration) of Vincristine and prednisone will be given throughout the first two years of therapy. Additionally, triple intrathecal (into spinal fluid) therapy (TIT) consisting of methotrexate, hydrocortisone, cytosine arabinoside will be given at the start of treatment and periodically through the first two years of therapy to prevent the spread of leukemia to the central nervous system (CNS). The vitamin Leucovorin will be given to prevent methotrexate toxicity. After week 25, during the continuation phase, all medications will be on an outpatient basis

The total duration of therapy is planned to be 2 1/2 years from initial diagnosis. If tests at that time indicate no evidence of leukemia, then all medications will be stopped and you (your child) will be followed closely to be sure that there is no evidence of return of the disease.

**Progress:** This study closed to patient accrual 15 Nov 99. No patients enrolled in this study in FY 00 at MAMC. One patient enrolled in this study at MAMC in FY 96 and another patient was accepted in transfer. Both continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 94/033	<b>Status:</b> Ongoing
<b>Title:</b> POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; COL Bruce A. Cook, MC; COL Stephen R. Stephenson, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 11/5/1993	<b>Est. Completion Date:</b> Jun 96	<b>Periodic Review:</b> 4/25/2000

**Study Objective:** (1) To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites, and (2) To analyze in a large group of patients with localized non-Hodgkin's lymphoma (by pooling data from POG #83314, #8719 and the current study) prognostic factors which may predict subgroups of patients with a poor prognosis within the subgroup of patients with localized NHL.

**Technical Approach:** After staging, subjects that qualify will receive Vincristine 1.5 mg/M2 (max 2 mg) IV q wk x 6 weeks, prednisone 40 mg/M2/day in 3 divided doses x 28 days, Adriamycin 40 mg/M2/day IV days 1 & 22, and Cyclophosphamide 750 mg/M2/day IV days 1 & 22. Fluid intake is to be > 3000 ml/M2 on day of treatment. Triple intrathecal chemotherapy (TIT) will be given on days 1, 8, and 22 to those with head and neck primaries.

On day 43, or when blood counts recover, the patient will receive Adriamycin 40 mg/M2 IV, Cyclophosphamide 750 mg/M2 IV, Vincristine 1.5 mg/M2 (max 2 mg) IV, and Prednisone 50 mg/M2 in 3 divided doses x 5 days

On day 64 and when blood counts have returned to normal following the prescribed induction and consolidation regimen, the patient will be assessed for remission status.

**Progress:** This protocol closed to patient accrual 2 Jul 99. Two patients were enrolled in this study at MAMC in FY 97. Both patients completed treatment and continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 96/096

**Status:** Completed

**Title:** POG 9315: A Phase III Study of Large Cell Lymphomas in Children and Adolescents; Compariosn of APO vs. APO + IDMTX/HDARA-C

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
4/19/1996

**Est. Completion Date:**  
Jun 99

**Periodic Review:**  
4/25/2000

**Study Objective:** (1) To study whether intermediate-dose methotrexate/high dose ARA-C (ID MTX/HRara-C), administered during the maintenance phase can improve the event-free survival (EFS) of patients with advanced-stage large cell lymphoma (LCL) and (2) to further characterize the immunophenotypic and morphologic correlates of pediatric LCL.

**Technical Approach:** Patients will be randomized at registration to Regimen A or B. Patients who present with CNS disease will go after induction directly to Regimen B. Induction for both regimens will be the same, with additional intrathecal for patients with CNS disease. Maintenance A consists of 8 cycles of ID MTX/HD Ara-C alternating with 5 cycles of VCR/6-MP/ADR/Pred and 2 cycles of VCR/6-MP/MTX/Pred; a total of 15 cycles given at 3 week intervals. Maintenance B consists of 5 cycles of ADR/V/6-MP/Pred followed by 10 cycles of MTX substitution for ADR; a total of 15 cycles will be given at 3 week intervals. Following completion of therapy, examinations will be every month for the first 6 months; thereafter every 3 months until year 2 off therapy and then every 6 months until 5 years off therapy, then annually. Cardiac exams after completion of therapy will be required during first, third and fifty years off treatment.

**Progress:** The Pediatric Oncology Group reported this study closed to further patient enrollment, 29 Sep 00, when it was determined that the statistical power was too low to make continuation of the study a viable option. One patient was enrolled in this study at MAMC in FY 97; however, she was transferred to a civilian hospital prior to her sponsor's separation from the military.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/168	<b>Status:</b> Ongoing
<b>Title:</b> POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 7/21/1995	<b>Est. Completion Date:</b> Jul 99	<b>Periodic Review:</b> 5/28/2000

**Study Objective:** (1) To assess the toxicity of the combination of Hydroxyurea (HU) and Ara-C combined sequentially with interferon-alpha 2b (IFN) in children with adult type chronic myelogenous leukemia (ACML), and (2) To determine the frequency and duration of hematologic and cytogenetic response, and the length of time needed to achieve response during two years of such treatment.

**Technical Approach:** Therapy will be divided into 2 induction phases and a consolidation phase. Induction 1: Therapy will begin with two, or possibly three, weekly courses of hydroxyurea and Ara-C. Each course will consist of treatment given on three consecutive days as follows: after consuming clear fluids only for breakfast, hydroxyurea will be taken by mouth. Two hours later, Ara-C will be administered intravenously over 15 minutes. This will be repeated on the second and third day of each course. Subjects will receive at least two courses, beginning days 1 and 8. If blood counts are still above certain values on day 15, a third course will be given. Induction 2: Once blood counts have adequately recovered from the above chemotherapy, IFN treatment will begin. Subjects will receive IFN given as a subcutaneous injection daily for 14 days. Consolidation: IFN will then be continued at this dosage every Monday, Wednesday and Friday. IFN therapy will be interrupted for at least one week, approximately every 6 weeks, for a threeday course of hydroxyurea/Ara-C. This six-week cycle (IFN three times weekly for five weeks followed by a course of hydroxyurea/Ara-C), will be repeated for a total treatment time of approximately two years, assuming a good response to treatment. Most therapy will be administered at home (IFN) or in the outpatient clinic (hydroxyurea/Ara-C), with the exception being the first course of hydroxyurea/Ara-C and the first few days of IFN therapy, for which hospitalization is recommended. Every effort will be made to continue treatment for at least 90 days. All patients who have signs of progressive (worsening) disease within the first 90 days will be evaluated for possible discontinuation of this therapy. All other patients will continue on treatment for a total of 24 months. For those patients continuing on therapy past 90 days, the treatment will be discontinued (prior to 24 months) if there are signs of progressive disease at any time; if there is no evidence of any improvement by six months or if side effects develop which cannot be tolerated even with reduction in the drug dosages. Therapy may also be stopped at any time if a suitable marrow donor has been found and the physician decides that bone marrow transplantation would be in the patient's best interest. If the patient is still on therapy and responding well after 24 months, then the physician may offer to continue therapy with IFN alone. This will be offered as further therapy, but it will not be part of this study. It is not known how many years interferon may be safely given. The dosage schedule described above is to be considered a guideline. It is very possible that modification will need to be made depending on the side effects encountered.

Routine blood tests will be done during the first four to six weeks of therapy (the "induction" phase), and then every one to two weeks while on therapy. A bone marrow aspirate and biopsy will be done prior to start of induction therapy, then twice more at about three month intervals, and then every six months thereafter unless removed from the study because of no response, progressive disease (increased severity), or bone marrow transplantation. A



Chromosomal analysis will be completed on each bone marrow aspirate to find out if the Philadelphia chromosome is present. Each bone marrow aspirate will be followed by an ultrasound study of the spleen in order to determine the size of the spleen.

**Progress:** This protocol was closed to patient accrual 27 Jan 99. One patient was enrolled in this study at MAMC in FY95. She was taken off study July 97 to pursue bone marrow transplant and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 94/092      **Status:** Ongoing

**Title:** POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG      **Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
4/1/1994

**Est. Completion Date:**  
Jun 99

**Periodic Review:**  
5/23/2000

**Study Objective:** (1) To improve the survival of patients with osteogenic sarcoma, (2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma, (3) To compare the results of a combined chemotherapeutic regimen (high-dose methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide, (4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery, (5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs, (6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma, (7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

**Technical Approach:** This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifoxfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherapy alone.

**Progress:** This protocol was closed to patient accrual 25 Nov 97 due to adequate patient enrollment. Two patients were entered in this study at MAMC in FY 96. One patient chose to discontinue treatment early. The other patient completed therapy. Both patients continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/087	<b>Status:</b> Ongoing
<b>Title:</b> POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 3/17/1995	<b>Est. Completion Date:</b> Jun 99	<b>Periodic Review:</b> 3/28/2000

**Study Objective:** (1) To estimate the complete response rate for HIV related malignancies treated with interferon (aIFN), and (2) The secondary objectives are to estimate the one year disease free survival and to evaluate the toxicity of aIFN alone or in combination with anti-retroviral therapy.

**Technical Approach:** This study will require all patients to be enrolled in POG 9182 and compliance with all specimen submission requirements of that protocol. The study will minimize additional tissue, CSF or blood sampling except as required for monitoring for toxicity and tumor response. This study will take advantage of the demonstrated antitumor and antiviral activity of aIFN alone or in combination with other antiretroviral agents to treat HIV positive children with refractory or newly diagnosed malignancies. As the duration of response is one of the goals of this study, responders will continue on therapy indefinitely. Patients on this study will be treated using a interferon by subcutaneous injection every day for 14 days; then if your child's/adolescent's evaluation allows further treatment he/she will receive a interferon three times a week. This treatment will need to be monitored by a treating physician and blood tests will be performed in order to insure that the treatment is well tolerated and that the dose is appropriate. For that purpose 10cc of blood will be taken once a week. The physician and/or staff will be checking closely to see if any of these side effects are occurring. Routine physical exams, laboratory tests and tests such as biopsy or bone marrow aspiration may be necessary to monitor the effect of the treatment. Side effects usually disappear after the treatment is stopped. In the meantime, the doctor may prescribe medication to keep these side effects under control.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 95/058	<b>Status:</b> Ongoing
<b>Title:</b> POG 9400: ALinC 16 Classification (C) Protocol			
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC			
<b>Department:</b> POG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC			
<b>Start Date:</b> 12/16/1994	<b>Est. Completion Date:</b> Dec 99		<b>Periodic Review:</b> 11/19/1999

**Study Objective:** (1) To continue to characterize the biologic findings of the acute lymphoblastic and undifferentiated leukemias (immunologic markers, ploidy (DNA index), karyotyping, morphology) and their relationship, as prognostic factors for attaining and maintaining remission, (2) To apply to therapy selection, the determination that ploidy and certain structural chromosomal abnormalities predict poor prognosis, (3) To evaluate the usefulness of PCR technique in detecting minimal residual disease in patients with disease demonstrating t ( 9; 2 2 ) or t ( 1; 19 ) chromosomal abnormalities. (optional), (4) To apply to therapy selection molecular testing for 11q23 translocation in infants < 12 months of age with acute lymphocytic leukemia, (5) To determine the roll of p53 and pl6 tumor suppressor genes in T-ALL. (optional), (6) Individual patient outcome will be compared with the leukemia cell proliferation response to ask if proliferation in response to a myeloid growth factor is associated with an increased risk of developing AML. (optional), (7) To determine risk group assessment using Fluorescent In-Situ Hybridization (FISH) screening for Trisomies 4 and 10 in Non-T, Non B ALL, and (8) To determine if drug sensitivity profiles of blast cells for three commonly used chemotherapeutic agents - Adriamycin, Methotrexate, and Cytarabine correlate with a) initial response b) subsequent development of relapse.

**Technical Approach:** A bone marrow aspirate (a needle stick in hip bone to draw marrow into syringe) will be done to prove or disprove diagnosis of leukemia. If leukemia is present, it is important to identity the exact type and subtype of leukemia, in order to plan treatment. This typing requires that several laboratory tests be run on the leukemia cells in the bone marrow. As we perform the bone marrow aspiration we will be removing enough bone marrow (about 2-1/2 teaspoons) to run the laboratory tests. We may also need to draw some blood (about 2-1/2 teaspoons) from a vein to send for studies. Some of these tests will be done here and some will be sent to reference laboratories in other Pediatric Oncology Group institutions for different kinds of special tests to identify the characteristics of the leukemia cells.

**Progress:** This study closed to patient enrollment 15 Nov 99. Ten patients have been enrolled in this study at MAMC, (2 in FY95, 1 in FY96, 1 in FY97, 2 in FY99 and 2 in FY00 and two patients accepted as transfers). Presently, 8 patients continue to be followed in this study in FY00 at MAMC following the transfer of 2 patients to other institutions.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 96/144

**Status:** Ongoing

**Title:** POG 9404: T-Cell #4 Intensive Treatment for T-Cell Acute Lymphoblastic Leukemia and Advanced Stage Lymphoblastic Non-Hodgkin's Lymphoma

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
7/19/1996

**Est. Completion Date:**  
Aug 04

**Periodic Review:**  
6/27/2000

**Study Objective:** (1) To determine, in a randomized trial, the effectiveness of high dose methotrexate (HD MTX) when added to a multi-agent chemotherapy backbone (DFCI 87-0001) proven effective in T-Cell acute lymphoblastic leukemias (T-ALL) and advanced stage non-Hodgkin's lymphoma (Lymphoblastic NHL), (2) to determine, in a randomized trial, the role of the cardioprotectant Zinecard (DZR) in preventing cardiotoxicity in children with T-ALL and advanced stage Lymphoblastic NHL receiving an anthracycline based regimen, (3) to study the biology of T-Cell lymphoid malignancies by accumulating data on the concurrent ALL classification study (POG 9400) and analyzing the data relative to outcome, (4) to evaluate the correlation of minimal residual disease with event-free survival utilizing the TAL 1 proto-oncogene, (5) to determine the role of p53 and p16 tumor suppressor genes in T-ALL, and (6) to determine if drug sensitivity profiles of blasts cells to Doxorubicin, methotrexate and cytarabine correlate with initial response and subsequent development of relapse.

**Technical Approach:** Patients will receive induction therapy (weeks 1-6), Vincristine every week for 4 weeks, prednisone for 21 days starting day 1 and doxorubicin on days 1, 2, and 22, with or without ZINECARD. During this phase, the drug methotrexate will be given on day 2. Patients will be randomized to receive high dose methotrexate on day 22. Intrathecal methotrexate, Ara-C and hydrocortisone will be given to prevent central nervous system disease throughout the entire three phases of treatment. Once remission has been achieved, patients will receive consolidation therapy (weeks 7-33). Drugs will be given in three week cycles (6-mercaptopurine for 14 days, Vincristine and doxorubicin on day 1 of the cycle, prednisone for 21 days) with or without ZINECARD. Asparaginase will also be given during the consolidation phase once a week during weeks 7-26. Patients who received high dose methotrexate on day 22 of induction will also receive it on weeks 7, 10 and 13 of consolidation. At weeks 22-24, all patients will receive radiation therapy to the brain. During continuation (weeks 34-108), patients will receive Vincristine, prednisone (every day for five days) and 6-MP (every day x 14 days) every three weeks. Methotrexate, will be given every week except during those weeks when patients receive intrathecal medications.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 95/059

Status: Ongoing

Title: POG 9405: ALinC #16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: POG

Facility: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

Start Date:  
12/16/1994

Est. Completion Date:  
Dec 99

Periodic Review:  
5/23/2000

**Study Objective:** (1) To determine in a randomized trial, the efficacy of a higher (2.5 gms/m<sup>2</sup>) versus standard (1 gm/m<sup>2</sup>) dose Methotrexate (MTX) infusion during consolidation. The major endpoint will be event free survival among those achieving a complete remission. Secondary comparisons will include site specific events and adverse drug reactions, (2) To determine in a randomized comparison, the efficacy of delivering oral 6-Mercaptopurine (6-MP) on a once versus twice daily schedule during continuation, (3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405 and 9406, and (4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

**Technical Approach:** In this research study, the subject will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as Prednisone, given orally (by mouth) for 28 days; Vincristine, given by a quick intravenous infusion (IV push) on days 1, 8, 15, and 22; L-Asparaginase, injected into a muscle (IM) on days 2, 5, 8, 12, 15, and 19. The drugs Methotrexate, Cytosine arabinoside (Ara-C), and hydrocortisone will be administered intrathecally (injected into the spinal fluid) at various intervals throughout both the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. After induction, the subject will be randomized to a specific regimen to include either standard or high dose IV Methotrexate and receiving oral 6-MP once or twice daily. During the period of consolidation (weeks 5-28), the subject will receive the drugs Methotrexate and 6-MP. The Methotrexate will be given at a standard or higher dose. In the first week, Methotrexate will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of Methotrexate. Immediately after the Methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive Methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days. This 2-week treatment will be repeated for 12 cycles. During the period of continuation (weeks 20-130), 6-MP will be given orally each day, and Methotrexate injected into a muscle (IM) once each week. Patients randomized onto regimens B & D will receive 6-MP orally twice daily. The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fail to achieve a complete remission during the induction phase of the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies.

**Progress:** This protocol closed to patient accrual 26 Dec 95 due to excessive neurotoxicity. Two patients were enrolled at MAMC. One patient was enrolled in this study at MAMC in FY95, and was taken off study but continues to be followed. The other patient enrolled in FY 96 was transferred to Beaumont Naval Medical Center.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 95/060

Status: Ongoing

Title: POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL)

Principal Investigator: LTC Kelly J. Faucette, MC

Department: POG

Facility: MAMC

Associate Investigator(s): MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Stephen R. Palmer, MC; LTC Shirley E. Reddoch, MC

Start Date:  
12/16/1994

Est. Completion Date:  
Dec 99

Periodic Review:  
11/19/1999

**Study Objective:** (1) To determine the efficacy of a 2.5 gm/m<sup>2</sup> dose versus 1 gm/m<sup>2</sup> does intravenous methotrexate infusions during intensified continuation therapy. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events and adverse drug reactions, (2) To determine whether intensified continuation therapy delivering pulses of Ara-C (3 gm/m<sup>2</sup> x 4 doses) with asparaginase rescue is superior to standard intensified continuation with pulses of VM-26/Ara-C. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events (including secondary AML) and adverse drug reactions, (3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406, and (4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

**Technical Approach:** In this research study, a child will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as prednisone, given orally for 28 days; Vincristine, given by a quick intravenous infusion on days 1, 8, 15, and 22; L-asparaginase, injected IM on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, cytosine, arabinoside (Ara-c), and hydrocortisone will be administered intrathecally at various intervals throughout the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. Daunomycin will be given on days 8, 15, and 22 intravenously. After the previous treatment, subjects will be randomized to a specific regimen to include either standard or high dose Methotrexate or low or high dose Ara-C. During the period known as consolidation, the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP) during weeks 5-6, 10-11, 15-16, 25-26, and 30-31. In the first week of each of these periods, methotrexate (either the standard or the intensified higher dose) will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days

At weeks 7, 17, and 27 the subject will receive Ara-C as a continuous infusion for 72 hours (higher dose) or injected under the skin (lower dose). VM-26 will be given as a 45-minute IV infusion before the start of Ara-C and on day 2 with standard dose Ara-C. If the subject receives intensified Ara-C, the subject will also receive the drugs PEG and G-CSF. PEG is a drug that may lessen the toxic effects of Ara-C, and G-CSF is used to increase the blood count to decrease the risk of infection

At weeks 12, 22, and 32, Ara-C will be infused over 72 hours as described above. Daunomycin (DNR) will be given as a 30-minute infusion before the start and at the end of the Ara-C. In addition to DNR/Ara-C, Vincristine is given IV on days 1 and 8, prednisone by mouth on days 1 and 7, and PEG-L-asparaginase IM on day 1

During the period known as continuation, weeks 35-130, standard dose 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once a week. The total time of planned therapy is 130 weeks (2 1/2 years)

The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study. Radiation therapy will be suggested if the subject has CNS leukemia at diagnosis

At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies.

**Progress:** This study closed to patient enrollment 15 Nov 99. No patients were enrolled in FY 00. One patient enrolled in this study in FY 96, however due to an adverse event during induction was taken off study and has since completed therapy. Another patient accepted in transfer from SUNY relapsed while on therapy and went on to have a bone marrow transplant. Both patients continue to be followed.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/089

**Status:** Ongoing

**Title:** POG 9421: Phase III Evaluation of Standard vs. High Dose ARA-C Induction Followed by the Randomized Use of Cyclosporine A As An MDR Reversal Agent, Compared to Allogeneic BMT, in Childhood AML

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; COL Bruce A. Cook, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
3/17/1995

**Est. Completion Date:**  
Jan 01

**Periodic Review:**  
4/25/2000

**Study Objective:** (1) To determine the effect of high dose vs. standard dose Ara-C induction on CR (clinical remission) and EFS (event free survival) in Childhood AML, (2) To compare EFS in Childhood AML after 3 cycles of consolidation with or without the MDR (multidrug resistance) modulator CSA (cyclosporine A), (3) To compare the EFS between patients genetically randomized between allogeneic BMT and chemotherapy, (4) To evaluate the impact of EFS of various clinical and laboratory factors such as cytogenetics and MDR expression, and (5) To confirm the superior response of Down syndrome patients utilizing standard induction and non-CSA containing consolidation, and identify specific biologic and pharmacokinetic characteristics in these patients.

**Technical Approach:** Phase III evaluation of standard vs. high dose Ara-C induction followed by the randomized use of Cyclosporine A as an MDR (multidrug resistant) reversal agent, compared to allogeneic BMT, in childhood AML. Patients will be randomized (assigned by chance, such as flipping a coin) at the time of diagnosis to receive either standard doses or high doses of ARA-C during the initial course of therapy. The chances of receiving any of the therapies is approximately equal. Later in the course of therapy, patients (according to how they were previously randomized) will or will NOT receive the drug Cyclosporine A in combination with the chemotherapy agents, Mitoxantrone and Etoposide. Patients with Down syndrome will not be randomized, but will receive the standard therapy. Earlier studies have shown the three year event-free survival rate for Down syndrome children significantly superior to children without Down syndrome using standard therapy. Also, for this reason Down syndrome patients will not receive Cyclosporine A. If a sibling who is matched for bone marrow transplantation, will receive bone marrow transplantation, which has been shown to be a more effective treatment in controlling AML compared to chemotherapy, providing that consent from the sibling donor can be obtained. If not a sibling donor, studies have shown chemotherapy is superior to matched unrelated donor BMT. However, should the patient choose to pursue an unrelated matched BMT instead of continuing with consolidation chemotherapy, the subject may discontinue the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may also be used for research studies.

**Progress:** This study closed to patient accrual, 15 Aug 99. Two patients continue to be followed at MAMC. One patient was accepted in transfer from WRAMC and the other patient was enrolled in FY 99.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/071

**Status:** Ongoing

**Title:** POG 9425: Advanced Stage Hodgkin's Disease, A Pog Phase III Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
3/21/1997

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
3/28/2000

**Study Objective:** (1) To test the efficacy of DBVE-PC, an intensive treatment regimen for advanced stage Hodgkins disease that administers doxorubicin, bleomycin, Vincristine, etoposide, prednisone and cyclophosphamide with G-CSF at 3 week intervals in a dose intensive manner (using cumulative drug doses that may minimize long term toxicity), followed by consolidative radiotherapy, (2) To tailor therapy based on rapidity of response in order to minimize cumulative drug dosages. Those in CR after 3 cycles of DBVE-PC will receive only low dose RT. Those who are not in CR will receive 2 additional cycles of DBVE-PC (+ low dose RT), (3) To determine, in a randomized trial, whether the addition of Dexrazoxane reduces pulmonary and cardiac toxicity of DBVE-based therapy without compromising response.

**Technical Approach:** Registered study patients will be randomized to receive or not to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 3 cycles of the drug combination etoposide, Vincristine, bleomycin, doxorubicin cyclophosphamide, prednisone combination with G-CSF in 3 week intervals. Patients will be restaged after receiving these three chemotherapy courses. Those showing large tumor response will go on to radiation therapy, while those showing partial response will receive 2 additional cycles of chemotherapy and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis after completion of therapy.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/054

**Status:** Ongoing

**Title:** POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
2/21/1997

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
2/22/2000

**Study Objective:** (1) To tailor chemotherapy courses based on the patients' initial response to therapy, (2) To examine the activity of variable courses of doxorubicin, bleomycin, Vincristine, and etoposide (DBVE) and low-dose involved field irradiation, (3) To monitor safety and feasibility of the response-dependent approach, and morbidity, immediate and long term toxicities of the above regimen, (4) To evaluate if limited therapy is adequate for patients with early response, (5) To examine if addition of Zinecard can reduce pulmonary toxicity while not significantly reducing response rate or event-free survival, and (6) To determine if the frequency and magnitude of myocardial injury during therapy, as measured by an elevation of cardiac Troponin-T in the serum, is reduced by the addition of Zinecard.

**Technical Approach:** Registered study patients will be randomized to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 2 courses of the four drug combination etoposide, Vincristine, bleomycin and doxorubicin at 28 day intervals. Patients will be restaged after receiving these two chemotherapy courses. Those showing remission will go on to radiation therapy, while those showing residual disease will receive 2 more courses of the four drug combination and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis.

**Progress:** This protocol closed to patient entry, 19 Sep 00. Two patients enrolled in this study at MAMC, one patient in FY 98 and the other patient in FY 00. Both patients continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 96/097	<b>Status:</b> Ongoing
<b>Title:</b> POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 4/19/1996	<b>Est. Completion Date:</b> Jul 02	<b>Periodic Review:</b> 4/25/2000

**Study Objective:** (1) To increase the survival rate of children with favorable histology Wilms tumor and other renal tumors of childhood, (2) to determine if loss of heterozygosity for chromosome 16q markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (3) to determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (4) to determine if increased DNA content in tumor cells is associated with a poorer prognosis, (5) to decrease the acute and long term morbidity of treatment of children with Wilms tumor, (6) to improve the survival of patients with unfavorable histology tumors including Wilms tumor with diffuse anaplasia and clear cell sarcoma of the kidney by using a new treatment regimen that includes etoposide and cyclophosphamide, (7) to improve survival of patients with malignant rhabdoid tumor of the kidney, (8) to study biology and pathology of patients who present with bilateral Wilms tumor, (9) to conduct hypothesis-driven trials led by diagnostic radiologists in order to develop guidelines, and (10) to establish a biological samples bank containing touch preparations, paraffin blocks, frozen tumor, normal kidney tissue, and serum and urine.

**Technical Approach:** This proposed therapeutic trial involves a number of experimental regimens that are designed either to reduce treatment for the subgroup of patients with the most favorable prognosis, or to intensify treatment for several subgroups with the least favorable prognosis. Patients will be stratified into the appropriate treatment regimens by age, size of tumor at diagnosis and staging of the tumor (Stages I-V) with favorable/unfavorable histology, including rhabdoid, clear cell sarcomas and Wilms tumor with diffuse or focal anaplasia. Treatment will include nephrectomy or surgical debulking of tumor, radiation therapy to abdomen and/or lungs, and appropriate chemotherapy regimens.

**Progress:** One patient was enrolled in this study at MAMC in FY 96 and was transferred to Portsmouth Naval Hospital. One patient was accepted in transfer from Tripler AMC and continues to be followed. No patients were enrolled in FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/090

**Status:** Ongoing

**Title:** POG 9442: National Wilms Tumor Late Effects Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
7/17/1998

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
6/27/2000

**Study Objective:** To determine (1) the frequency of Wilms tumor and other cancers in family members of Wilms tumor patients in order to estimate the recurrence risk in siblings and offspring; test the plausibility of specific genetic modes of inheritance in homogeneous subgroups; and identify familial cancer syndromes (if any) that may involve Wilms tumor, (2) To determine fertility rates of Wilms tumor patients and rates of perinatal mortality, low birth-weight and adverse pregnancy outcomes in relation to the type and amount of cancer treatment received in childhood, (3) To estimate the rates of selected congenital defects and of specified single gene disorders (sentinel phenotypes) in the offspring of Wilms tumor patients, (4) to estimate the rates of second malignancy neoplasms in relation to the dosage of radiation therapy and the use of specific chemotherapeutic agents (actinomycin D, doxorubicin, cytoxan and etoposide) received in childhood, (5) to compare the incidence rate of congestive heart failure among Wilms tumor survivors in relation to the dose of radiation therapy received to abdomen and/or lungs and to the use of specific chemotherapeutic agents.

**Technical Approach:** The large number of Wilms tumor survivors ascertained by the NWTS during its first twenty years of operation constitutes an ideal cohort for the study of familial risk and late effects of treatment. Four protocol studies have been conducted; treatment protocols and results for the first three studies have been published. A large fraction of the total national U.S. incidence of Wilms tumor has been registered on these studies, probably as much as 70% of an estimated 450-500 cases occurring nationally since 1980. Over 2,500 children who were followed on NWTS treatment protocols have now survived 5 or more years since their original diagnosis. Many of those treated more than a decade ago have reached sexual maturity, so that their reproductive history and the status of their offspring may be evaluated by entry into this study.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 96/039	Status: Completed
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**Title:** POG 9457: Intensive Therapy with Growth Factor Support for Patients with Ewing's Tumor Metastatic at Diagnosis

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Luke M. Stapleton, MC; LTC Kenneth A. Bertram, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
12/15/1995

**Est. Completion Date:**  
Sep 99

**Periodic Review:**  
11/19/1999

**Study Objective:** (1) To evaluate the response rate, and duration of response in patients with Ewing's tumor, metastatic at diagnosis, treated with maximally intensified therapy, (2) To evaluate the response to new agents utilized in an upfront window. Initially, topotecan will be used as a single agent. When the maximally tolerated dosages of the combination of topotecan and cyclophosphamide are available, the combination will be employed, (3) To assess the role of surgical treatments with regard to local control of primary and metastatic sites and disease course, (4) To determine whether individual variability in ifosfamide and cyclophosphamide metabolism correlated with toxicity and/or response, and (5) To evaluate the rise in the absolute neutrophil count following one dose of G-CSF just prior to a chemotherapy cycle as a measure of bone marrow reserve and subsequent myelosuppression.

**Technical Approach:** In the absence of effective new agents in Ewing's Tumor, attempts to increase the rate of cure have recently centered around increasing dose intensity. Ifosfamide will be used at a dosage level 25% higher than that currently being used, for the first 3 cycles. The dosage will be reduced for the 2 continuation cycles. Cyclophosphamide will also be used in increased dosage with Vincristine and adriamycin. This study will encourage the use of surgery for local control, with irradiation of the primary tumor bed, unresectable primary tumors and selected metastatic sites. Topotecan is a camptothecin, a topoisomerase I inhibitor. Initially, this study will use 2 cycles of single agent topotecan 3 weeks apart. At least 14 patients will be registered. When the maximum tolerated dosages of the combination of topotecan and cyclophosphamide are available, subsequent patients will be treated with the combination.

**Progress:** This protocol closed to patient entry 31 March 2000, as patient accrual requirements had been met. No patients were enrolled at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 96/035      **Status:** Ongoing

**Title:** POG 9490: Topotecan Followed by Multimodal, Multiagent Therapy for Children and Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
11/17/1995

**Est. Completion Date:**  
Jun 97

**Periodic Review:**  
5/23/2000

**Study Objective:** (1) To evaluate the toxicity of the topoisomerase I inhibitor, topotecan, when given alone at a maximum tolerated dose by bolus injection daily X 5 days/course for 2 courses to untreated children and adolescents with Stage IV and/or Clinical Group IV rhabdomyosarcoma, all patients with metastatic disease, (2) To estimate the response rate (complete or partial) of such patients to topotecan, and (3) To evaluate the toxicity of a new chemotherapy combination comprising topotecan, cyclophosphamide, and Vincristine (VTC) given in alternating cycles with Vincristine, actinomycin D, and cyclophosphamide (VAC) to patients who have achieved an objective response partial response (PR) or complete response (CR) to topotecan.

**Technical Approach:** Patients with rhabdomyosarcoma, clinical stage IV disease will receive Topotecan upfront at 2.0 mg/M<sup>2</sup>/day X 5 IV. Following evaluation, patients with partial response or complete response will go on to VAC treatment, alternating with VTC treatment. Those with stable or progressive disease will proceed to VAC alone. Radiation therapy will begin following evaluation at week 15 in conjunction with Vincristine and cyclophosphamide. Continuation therapy begin following evaluation at week 25 with VAC/VTC for patients showing PR and CR.

**Progress:** This protocol closed to patient accrual 1 Nov 96. One patient was enrolled in this study at MAMC in FY 96 and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 97/089      **Status:** Completed

**Title:** POG 9553: A Phase II of Neoadjuvant Vincristine, Ifosfamide, Doxorubicin, and G-CSF in Children with Advanced Stage Non-rhabdomyosarcoma Soft Tissue Sarcomas

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG      **Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
4/18/1997

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
4/25/2000

**Study Objective:** (1) To estimate the response rate to the combination of Vincristine, ifosfamide, and doxorubicin (VID), with G-CSF support, in children with newly diagnosed inoperable or metastatic non-rhabdomyosarcoma soft tissue sarcomas, (2) To estimate the 2-year survival and event-free survival of children treated with VID in combination with radiotherapy and/or surgery, and (3) To establish a bank of frozen tissue (tumor and peripheral blood) for use in further molecular studies.

**Technical Approach:** Registered study patients will receive the three drug combination Vincristine, Ifosfamide, and Doxorubicin; two courses within a 6 week period. Cyclophosphamide will be substituted for those patients who cannot tolerate Ifosfamide. Patients will then be evaluated for response. If the tumor shrinks, patients will go on to XRT/chemotherapy, with or without prior surgical resection at this time. If the tumor has grown or stayed the same, patients will be taken off study treatment and offered other therapy. After XRT and chemotherapy, patients will be reimaged and another six weeks of chemotherapy will be given at this time unless the tumor has grown or come back.

**Progress:** This study closed to patient enrollment, 30 Jun 00, due to adequate accrual. No patients were enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 96/120	<b>Status:</b> Ongoing
<b>Title:</b> POG 9605: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 5/17/1996	<b>Est. Completion Date:</b> Jul 03	<b>Periodic Review:</b> 5/23/2000

**Study Objective:** (1) To determine in a randomized trial whether the addition of 6 months of delayed intensification with divided dose oral methotrexate (ddMTX) improves event-free survival (EFS) of children with standard risk acute lymphoblastic leukemia, (2) to determine in a randomized trial the effect on EFS of delivering oral 6-mercaptopurine (6-MP) on a divided (twice daily) vs once a day schedule, during delayed intensification and continuation, (3) to study how laboratory data from POG 9400 correlates with outcome by pooling studies 9201, 9405, 9605, and 9406, (4) to assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy, and (5) to describe the occurrence of elevated transaminases and correlation of these with outcome.

**Technical Approach:** This treatment protocol involves 130 weeks of chemotherapy beginning with standard induction therapy of generally 4 (but up to 6) weeks of chemotherapy consisting of Vincristine, prednisone, and L-asparaginase plus triple intrathecal therapy of combined methotrexate, hydrocortisone and Ara-C. Post induction, the treatment is divided into consolidation, intensification, and maintenance phases of therapy. Registration on study occurs post induction therapy at which time patients are randomized to receive 1 of 4 regimens which vary beginning in the intensification phase of therapy.

**Progress:** This protocol is closed to patient entry 15 Nov 99. No patients were enrolled in FY 00. One patient enrolled in this study at MAMC in FY 96 was transferred to WRAMC. Three patients have been accepted as transfers from other POG institutions. Two patients were enrolled in FY 99. Six patients are currently being followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/045	<b>Status:</b> Ongoing
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**Title:** POG 9631: A Phase II Feasibility Study of Oral Etoposide Given Concurrently with Radiotherapy Followed with Dose Intensive Adjuvant Chemotherapy for Children with Newly-Diagnosed High Stage Medulloblastoma

**Principal Investigator:** LTC Kelly J. Faucette, MC

<b>Department:</b> POG	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
2/23/1999

**Est. Completion Date:**  
Feb 05

**Periodic Review:**  
2/22/2000

**Study Objective:** (1) To estimate the response rate and toxicity of children with newly diagnosed high-stage medulloblastoma who are treated with 2 cycles of oral etoposide, given concurrently with radiation therapy, (2) To compare the response rate and toxicity of these patients to historical control patients registered on POG study # 9031 TRT 2 (RT alone followed by adjuvant chemotherapy), (3) To estimate the 2-year event-free survival and overall survival of patients treated with 2 cycles of oral etoposide, given concurrently with radiation therapy, (4) To compare the 2-year event-free survival and overall survival of these patients to historical control patients registered on POG study # 9031, and (5) To evaluate the toxicity of dose intensive chemotherapy following craniospinal irradiation using oral etoposide, cisplatin, cyclophosphamide and Vincristine.

**Technical Approach:** The goal of this study is to maximize response to initial therapy using oral etoposide concurrently with radiotherapy in children with newly diagnosed high stage medulloblastoma. Adjuvant therapy will continue after radiation using dose intensive chemotherapy.

**Progress:** No patients enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/065

**Status:** Ongoing

**Title:** POG 9641: Primary Surgical Therapy for Biologically Defined Low-Risk Neuroblastoma; A Pediatric Oncology Group Children's Cancer Group, Phase III, Intergroup Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
3/20/1998

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
3/28/2000

**Study Objective:** (1) To determine if low risk INSS stage 2A/2B asymptomatic neuroblastoma patients treated with surgery alone will have a three year survival (S) rate of 95%, (2) To determine if low risk INSS stage 1 asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (3) To determine if low risk INSS stage 4S asymptomatic neuroblastoma patients treated with surgery alone will have a three year S rate of 95%, (4) To estimate the response and 3 year event-free survival (EFS) rates of symptomatic patients with chemotherapy, (5) To estimate the EFS and S rates in patients who relapse or progress after initial treatment with surgery alone, (6) To determine the acute and long-term morbidity/toxicities associated with treating low-risk neuroblastoma with surgery alone or with surgery and chemotherapy, (7) To further define and evaluate the prognostic importance of other biologic factors as determined on studies POG #9047 (or its successor), CCG #B973, and by International Neuroblastoma Risk Group criteria, (8) To collect resource utilization data regarding number of hospital days, the extent of transfusion support, and the use of diagnostic imaging, and to compare these with historical CCG study 3881 data.

**Technical Approach:** Patients in this study will be stratified by stage and extent of disease to either surgery alone or surgery with chemotherapy. Further studies done on patient's tumor specimens may change their classification to "intermediate" or "high" risk neuroblastoma, in which case they will be taken off study and more intensive chemotherapy will be administered.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/064	<b>Status:</b> Completed
<b>Title:</b> POG 9701 (A09701): A Phase II Study of Temodal (SCH 52365; Temozolomide, IND #52797) in Children and Adolescents with Recurrent Central Nervous System (CNS) Tumors		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC		
<b>Start Date:</b> 3/20/1998	<b>Est. Completion Date:</b> Jun 03	<b>Periodic Review:</b> 3/28/2000

**Study Objective:** To determine the response rate to Temodal in several strata of recurrent CNS tumors of childhood and to further assess the toxicity of Temodal in a larger group of patients treated at the recently defined maximally tolerated dose (MTD).

**Technical Approach:** The study is divided into two treatment strata; prior history of craniospinal (CSI) or total spinal radiotherapy. Patients without prior CSI will receive Temodal(r) 200 mg/m<sup>2</sup>/day orally for five consecutive days, following overnight fast. Patients may not eat for two hours after administration of capsules. Subsequent courses may begin on day 28, if all toxicities have resolved. Patients with prior CSI will receive Temodal(r) 180 mg/m<sup>2</sup>/day orally for five consecutive days, following overnight fast. Patients may not eat for two hours after administration of capsules. Subsequent courses may begin on day 28, if all toxicities have resolved. Patients benefiting from Temodal(r) after 2 courses (patients with stable disease or a response) may continue up to 10 additional courses. Treatment must be stopped when disease progresses or when a total of 12 total courses of Temodal(r) have been administered.

**Progress:** This study closed to patient enrollment 29 Oct 99. One patient enrolled in this study at MAMC in FY 98, now deceased, completed 12 courses of therapy (study requirements) and was allowed to continue Temozolomide for 14 courses before disease progression and he was taken off study.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/066

**Status:** Ongoing

**Title:** POG 9720: Idarubicin and Cladribine in Recurrent and Refractory Acute Myeloid Leukemia: A Pediatric Oncology Group Phase II Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
3/20/1998

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
3/28/2000

**Study Objective:** (1) To determine the CR rate of the combination of Idarubicin (IDA) and Cladribine (CDA) in patients with recurrent AML, (2) To determine the CR rate of the combination of IDA and CDA in patients with primary refractory AML, (3) To determine the CR rate of the combination of IDA and CDA in patients with recurrent or primary refractory secondary AML and myelodysplastic syndromes (not related to Down's Syndrome), (4) To determine the toxicities of the combination of IDA and CDA, and (5) To define the pharmacokinetics of CDA administered as a 2 hour infusion.

**Technical Approach:** Eligible patients will be stratified and receive a five day treatment consisting of IV Idarubicin daily for 3 days and IV Cladribine, 2 hours daily for 5 days. Twenty-four hours after completion of chemotherapy, patients will begin daily subcutaneous injections of G-CSF until blood counts stabilize. A bone marrow aspirate will be done at 3 weeks to assess response. A second course may be given. If patients have progressive disease they will be taken off study.

**Progress:** No patients enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/032	<b>Status:</b> Ongoing
<b>Title:</b> POG 9900: ALinC 17 Classification (C) Protocol, A POG Non-therapeutic Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Jan 05	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To provide the clinical and laboratory data necessary for placing each patient with ALL onto proper therapeutic trial, and (2) to provide an administrative base to capture classification data for correlative studies in ALL treatment protocols and series of historical protocols.

**Technical Approach:** At the time of diagnostic evaluation which includes bone marrow aspiration and/or biopsy, 20 ml of bone marrow and 25 ml of peripheral blood will be collected and processed for local laboratory studies and submission to the following POG reference laboratories: 1. Johns Hopkins University for Immunophenotyping. 2. University of New Mexico (UNM) for DNA Index, FISH, Molecular testing, Cell banking. 3. Medical College of Wisconsin for Glucocorticoid receptors. 4. University of Texas Southwestern Medical Center for Homocysteine Children's Hospital of Michigan for Drug sensitivity profiles. 5. MUSC - Children's Hospital for Drug sensitivity profiles. UCSD Medical Center for Tumor suppressor gene studies. The data captured on this protocol will be used in the therapeutic trials, in cross era analysis, and in international collaborations to further define the prognostic importance of biologic features in ALL.

**Progress:** One patient was enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/077

**Status:** Ongoing

**Title:** POG 9904: ALinC 17 Protocol for Patients with Newly Diagnosed Low Risk Acute Lymphoblastic Leukemia (ALL), A POG Phase III Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
5/12/2000

**Est. Completion Date:**  
May 04

**Periodic Review:**  
N/A

**Study Objective:** (1) In conjunction with POG 9905, to compare short MTX infusion (2g/m<sup>2</sup> over 4 hours) with a longer infusion (1g/m<sup>2</sup> over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity

(2) to determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL, (3) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (4) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

**Technical Approach:** This protocol will randomize between the 4-hour and 24 hour methotrexate infusion and for patients with TEL/AML1 gene, between standard and delayed intensification. Data from POG 9904 and 9905 will be pooled for statistical analysis of efficacy and toxicity. This study will determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). Induction will include three or four drugs (dependent on initial risk classification POG 9900).

**Progress:** No patients have been enrolled in this study in FY 00 at MAMC. In response to reported SAEs from other institutions concerning sepsis, Amendment #1 was IRB approved replacing dexamethasone with prednisone during induction therapy.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/076	<b>Status:</b> Ongoing
<b>Title:</b> POG 9905: ALinC 17 Protocol for Patients with Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL), A POG Phase III Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC		
<b>Start Date:</b> 5/12/2000	<b>Est. Completion Date:</b> May 04	<b>Periodic Review:</b> N/A

**Study Objective:** 1) To determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL. This objective will also be assessed as part of POG protocol 9904; 2) In conjunction with POG 9904, to compare short MTX infusion (2g/m<sup>2</sup> over 4 hours) with a longer infusion (1g/m<sup>2</sup> over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity; 3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): (a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; (b) Marrow morphology on day 8, and; (c) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples on day 29 and after consolidation; 4) Using a case control design, quantitate MRD with flow cytometry and molecular techniques, to determine whether late relapse correlates with a given level of MRD in marrow samples obtained and banked at the completion of therapy. To analyze samples obtained at relapse to ascertain whether markers of MRD remain constant i.e., if a relapse not "predicted" by high levels of MRD in remission samples, is it because of a change in the identified markers; 5) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction); 6) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

**Technical Approach:** This study will utilize a 2 x 2 factorial design to answer two randomized questions. The standard arm will recapitulate regimen A of the current POG protocol for standard risk patients. Induction will include three or four drugs (dependent on initial risk classification POG 9900) and consolidation will include 24-hour MTX infusions, at one gram per square meter, given every three weeks for a total of six doses. The two randomizations will assign patients to receive therapy with or without the delayed intensification and receive the IV MTX as a 2 gm/m<sup>2</sup> infusion over four hours versus a one gram per m<sup>2</sup> infusion over 24 hours. Intensive continuation will include 4 cycles of therapy with each 12 week cycle including 6 courses of divided dose oral MTX, nightly 6-MP, a dose of intrathecal MTX and a pulse of Vincristine and dexamethasone. Standard continuation therapy includes weekly MTX, daily 6-MP and Vincristine/dexamethasone pulses every 16 weeks. Dexamethasone replaced prednisone in the 9705 pilot study, and will be utilized here because of better CNS penetration and data suggesting that its use enhance event-free survival. The current POG study for standard risk patients includes a randomization to single versus twice daily dosing of oral 6-MP, based on the concept that duration of exposure is critical to anti-metabolite efficacy. This study includes only the traditional single nightly dose. Should the results of the open trial suggest an advantage to the use of divided dose 6-MP, this protocol will be amended.

**Progress:** One patient was enrolled in this study in FY 00 at MAMC with no adverse events reported. In response to reported SAEs from other institutions concerning sepsis, Amendment #1 was IRB approved replacing dexamethasone with prednisone during induction therapy.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/075

**Status:** Ongoing

**Title:** POG 9906: ALinC 17 Protocol for Patients with Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL), Evaluation of the Augmented BFM Regimen, a POG Phase III Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
5/12/2000

**Est. Completion Date:**  
May 04

**Periodic Review:**  
N/A

**Study Objective:** 1) To determine for patients at high risk for treatment failure if the augmented Berlin-Frankfurt-Munster (A-BFM) therapy is superior to ALinC 14/15 therapy, on the basis of historical controls; 2) To determine if minimal residual disease at the end of induction is predictive of an inferior prognosis; 3) To determine the correlation between event-free survival (EFS) and the following measures of minimal residual disease (MRD)/early response (ER): a) the rate of peripheral blast count disappearance and the absolute blast count on day 8 as determined morphologically, by flow cytometry and using molecular techniques; b) Marrow morphology on days 8, and 29; 4) MRD as determined by flow cytometry and molecular techniques on bone marrow and peripheral blood samples and at the end of induction and therapy and (5) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction)

5. To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis

6. To give Pediatric Oncology Group (POG) investigators experience with BFM-type regimens as these will likely play a major role in Children's Oncology Group (COG) protocols of the future.

**Technical Approach:** The regimen as defined by POG 9906 will represent a modified version of CCG augmented BFM for patients at high risk for treatment failure as defined by ALinC 17 clinical and biological criteria. Routine whole brain irradiation will not be used. Instead we will rely on intrathecal chemotherapy, except for those with established CNS disease at diagnosis. However, the augmented BFM results remain unsatisfactory for subsets of patients in the following categories: Philadelphia chromosome positive, hypodiploid (<45) modal chromosome number, and M-3 marrow at day 29. Both CCG and POG analyses concur that these groups, comprising approximately 3-4% of newly diagnosed patients with A.L.L., have an EFS <45%. These cases, henceforth classified as Very High Risk, will be entered on a separate combined POG/CCG (COG) trial evaluating new chemotherapy and marrow transplant strategies. Risk group assignment will be determined otherwise by the method of using age, WBC, CNS status, DNA index, and molecular and cytogenetic criteria as established for POG ALinC 17 classification protocol.

**Progress:** No patients were enrolled onto this study in FY 00 at MAMC. In response to reported SAEs from other institutions concerning sepsis, Amendment #1 was IRB approved replacing dexamethasone with prednisone during induction therapy.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/100

**Status:** Ongoing

**Title:** POG A3961: Treatment for Infants and Children with Intermediate Risk Neuroblastoma: A Pediatric Oncology Group/Children's Cancer Group Phase III Intergroup Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 07

**Periodic Review:**  
N/A

**Study Objective:** (1) To determine that Intermediate Risk Neuroblastoma with favorable biology will have a >90% event free survival (EFS) and survival (S) with a short course of chemotherapy (4 cycles) over 84 days without primary radiation therapy, (2) To determine that Intermediate Risk Neuroblastoma with unfavorable biology will have a >90% (EFS) with a longer course of chemotherapy (8 cycles) over 168 days without primary radiation therapy, and (3) To determine the acute and long term morbidity/toxicities associated with treating Intermediate Risk Neuroblastoma with surgery and chemotherapy.

**Technical Approach:** This study is an intergroup Phase III prospective nonrandomized trial to evaluate reduced therapy for intermediate risk neuroblastoma based on clinical and selected biologic, prognostic variables in order to maintain event free survival and survival, and minimize both acute and long-term morbidity in this group of patients. Either prior to or after study entry, patients will undergo an operation to remove as much of the primary tumor and involved lymph nodes as can be safely accomplished with minimum morbidity. Intermediate risk patients with favorable biology will receive 4 cycles of chemotherapy. Second surgery will be done for all patients not in complete remission following recovery from the 4th cycle of chemotherapy. Intermediate risk patients with unfavorable biology will continue with an additional 4 cycles of chemotherapy for a total of 8 cycles. At the conclusion of 8 cycles, the patient shall undergo second surgery. Radiotherapy will be administered to the site of viable residual disease after completion of 8 weeks of chemotherapy and second look surgery for selected intermediate risk INSS Stage 3 or 4 neuroblastoma patients with unfavorable biology.

**Progress:** No patients have been enrolled in this study in FY00 at MAMC, however a patient transfer is pending from Kansas City, MO.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/139

**Status:** Ongoing

**Title:** POG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III Intergroup CCG/POG Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
9/26/2000

**Est. Completion Date:**  
Sep 07

**Periodic Review:**  
N/A

**Study Objective:** (1) To compare the event free survival and survival in patients with disseminated lymphoblastic lymphoma treated on four regimens. (NHL/BFM-95 vs. CCG BFM), (2) To determine if treatment with a regimen without high dose methotrexate will maintain the same excellent disease free survival obtained with NHL/BFM-90, (3) To determine if intensification with anthracycline and cyclophosphamide improves disease free survival, (4) To collect outcome data on uniformly treated patients with localized disease or CNS positive disease, and (5) To determine if rapid reduction in tumor volume as defined by chest radiography and CT is predictive of improved outcome.

**Technical Approach:** Patients with disseminated (Murphy stage III or IV) lymphoblastic lymphoma without evidence of CNS disease will be randomized to one of four treatment regimens: Standard CCG BFM (regimen A1); CCG BFM intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen A2); Standard NHL/BFM-95 (regimen B1); or NHL/BFM-95 intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen B2). Patients with disseminated lymphoblastic lymphoma positive for CNS disease will be assigned to the intensified NHL/BFM-95 arm (regimen B2) with delayed radiation therapy. Patients with localized lymphoblastic lymphoma (Murphy stage I or II) will be assigned to the standard CCG BFM arm without additional intrathecal methotrexate (regimen AO). The duration of each treatment arm is 2 years and consists of Induction, Consolidation, Interim Maintenance, Delayed Intensification, and Maintenance therapies.

**Progress:** This protocol recently received review and approval by the IRB; however, it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/138	<b>Status:</b> Ongoing
<b>Title:</b> POG A9952: Chemotherapy for Progressive Low Grade Astrocytoma in Children Less Than Ten Years Old			
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC			
<b>Department:</b> POG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC			
<b>Start Date:</b> 9/26/2000	<b>Est. Completion Date:</b> Sep 07		<b>Periodic Review:</b> N/A

**Study Objective:** To compare the event-free survival as a result of treatment with both carboplatin and Vincristine (CV) or a combination of thioguanine, procarbazine, CCNU, and Vincristine (TPCV).

**Technical Approach:** After as complete as possible surgical resection, without causing increased neurological deficits, a child will be followed without further intervention until signs of progression are observed. Children with progressive symptoms due to tumor and minimal surgery are also eligible without initial follow-up. Children with NF and definitive progression of optic pathway tumors can be entered without surgery. At registration children will be randomly assigned to either CV or TPCV chemotherapy. All children with NF will be non-randomly assigned to CV. All children will be followed until signs of definite tumor progression. The children will not be taken off chemotherapy for stable disease since this may be a desirable outcome.

**Progress:** This protocol recently received review and approval by the IRB; however it has not yet received final approval to begin subject enrollment at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/088

**Status:** Ongoing

**Title:** POG A9961: A Phase III Prospective Randomized Study of Craniospinal Radiotherapy Followed by One of Two Adjuvant Chemotherapy Regimens (CCNU, CDDP, VCR, or CPM, CDDP, VCR) in Children with Newly-Diagnosed Average Risk Medulloblastoma

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**

4/18/1997

**Est. Completion Date:**

Apr 03

**Periodic Review:**

4/25/2000

**Study Objective:** (1) To determine if a cyclophosphamide arm will increase the rate of progression-free survival compared to a CCNU containing arm for children with average-risk medulloblastoma, (2) To determine the progression-free survival and overall survival of children treated with craniospinal (2340 cGy) and local boost radiotherapy (3240 cGy) for a total dose of 5580 cGy, and adjuvant Vincristine, CCNU and cisplatin chemotherapy, (3) To determine the progression-free survival and overall survival of children treated with craniospinal (2340 cGy) and local boost radiotherapy (3240 cGy) for a total dose of 5580 cGy, and adjuvant Vincristine, cyclophosphamide and cisplatin chemotherapy, (4) To determine the long-term neurocognitive, endocrinologic and cardiopulmonary sequelae of radiotherapy plus adjuvant chemotherapy in children with average-risk medulloblastoma treated with 2340 cGy of craniospinal radiation therapy, local boost radiotherapy, and either one of two drug regimens and to determine if the replacement of CCNU with cyclophosphamide will alter the incidence and degree of sequelae experienced, (5) To determine if cellular/biologic parameters, including tumor molecular genetic analysis, DNA ploidy, mitotic activity markers and immunohistochemical analysis are correlated with progression-free survival, survival and the pattern of disease relapse in children with average-risk medulloblastoma, and (6) To determine the utility of routine MR surveillance studies of the head and spine to detect subclinical recurrent disease.

**Technical Approach:** Following surgery, patients will be randomized to receive Regimen A or B of treatment. Both regimens will include 2340 cGy of craniospinal radiation and 3240 cGy of boost radiation directly to the primary tumor with weekly Vincristine doses. Six weeks following the completion of radiotherapy, patients will begin 8 cycles of maintenance chemotherapy for Regimen A (CCNU, cisplatin and Vincristine) or Regimen B (cyclophosphamide, cisplatin and Vincristine).

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 97/090                      **Status:** Completed

**Title:** POG D9501: Topotecan and Cyclophosphamide, Followed by Multimodel, Multiagent Therapy for Children & Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG    **Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Shirley E. Reddoch, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
4/18/1997

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
4/27/1999

**Study Objective:** (1) To evaluate the toxicity of cyclophosphamide and the topoisomerase I inhibitor, topotecan, when given together by 30 minute infusion daily x 5 days/course for 2 courses to untreated children and adolescents with Stage IV and/or Clinical Group IV rhabdomyosarcoma, all patients with metastatic disease, (2) To estimate the response rate (complete or partial) of such patients to cyclophosphamide and topotecan, (3) To evaluate the toxicity of a new chemotherapy combination comprising Vincristine (VCR), cyclophosphamide, and topotecan given in alternating cycles with Vincristine, dactinomycin, and cyclophosphamide (VAC) to patients who have achieved an objective response, partial response (PR) or complete response (CR) to topotecan.

**Technical Approach:** Patients with advanced stage rhabdomyosarcoma will receive two courses of Topotecan & Cyclophosphamide upfront. Following evaluation patients with partial response (PR) or complete response (CR) will go on to VAC treatment, alternating with VTC treatment. Those with stable or progressive disease will proceed to VAC alone. Radiation therapy will begin following evaluation at week 15 and in conjunction with Vincristine and cyclophosphamide. Continuation therapy begins following evaluation at week 25 with VAC/VTC for patients showing PR and CR; and VAC alone for patients with stable or progressive disease. Patients will be evaluated again at week 44.

**Progress:** This protocol was closed to patient entry, 1 Aug 99, as patient accrual requirements had been met. No patients were enrolled at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/145

**Status:** Ongoing

**Title:** POG D9602: Actinomycin D and Vincristine with or without Radiation Therapy for Newly Diagnosed Patients with Low-Risk Rhabdomyosarcoma or Undifferentiated Sarcoma: An IRS-V Protocol

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC; LTC Stephen R. Palmer, MC

**Start Date:**  
9/19/1997

**Est. Completion Date:**  
Jul 03

**Periodic Review:**  
8/22/2000

**Study Objective:** (1) Treatment of IRS-V low-risk patients with actinomycin D (AMD) and Vincristine (VCR), plus local radiotherapy (XRT) for microscopic or gross residual tumor, will result in a failure-free survival rate of 88% at 2 years and an overall survival rate of about 95% at 5 years from initial diagnosis, (2) Treatment of IRS-V low-risk patients with alveolar rhabdomyosarcoma or undifferentiated sarcoma with Vincristine and actinomycin D plus cyclophosphamide (collectively called VAC) will result in a failure-free survival rate of greater than or equal to 70% at two years and an overall survival rate of about 80-90% at 5 years, and (3) Reduction in radiation therapy dose for patients with Clinical Group II disease to 36 Gy (from 41.3 Gy) and for Group III patients with orbital disease to 45 Gy (from 50-S' Gy) will result in local control rates of about 90%.

**Technical Approach:** Patients in Group I have no residual tumor following surgery and will receive no radiation therapy. Patients in Group II have microscopic residual tumor and will receive radiation therapy at a dose lower than the current standard. Patients in Group III, orbit tumor only, have visible residual tumor after biopsy and will receive radiation therapy. The results will be compared to current intergroup rhabdomyosarcoma study results

All patients will begin chemotherapy with the two-drug combination of Vincristine and actinomycin D, given over a 3-week period while their tumor specimen is being classified at the IRS Group Pathology Center in Columbus, Ohio

Patients whose tumor is classified as embryonal or botryoid rhabdomyosarcoma will continue to receive Vincristine and actinomycin D, given at weeks 12 through 21, 24 through 33, and 36 through 45

Patients whose tumor is classified as alveolar rhabdomyosarcoma or undifferentiated sarcoma will have the chemotherapy drug cyclophosphamide added to the combination of Vincristine and actinomycin D, given at weeks 3, 6, 9, 12, 15, 18, 24, 27, 30, 36, and 42. Cyclophosphamide will be added on Week 0 for these patients who show molecular genetic or cytogenetic evidence of the t(2;13) or t(1;13) translocation, or the PAX 3-FRHR or PAX 7-FRER gene fusion product.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/051	<b>Status:</b> Ongoing
<b>Title:</b> POG D9802: A Phase II "Up Front Window Study" of Irinotecan (CPT-11) Followed by Multimodal, Multiagent Therapy for Selected Children and Adolescents with Newly Diagnosed Stage 4/Clinical Group IV Rhabdomyosarcoma, An IRS-V Study			
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC			
<b>Department:</b> POG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC			
<b>Start Date:</b> 2/22/2000	<b>Est. Completion Date:</b> Feb 06		<b>Periodic Review:</b> N/A

**Study Objective:** (1) To estimate the response rate associated with two cycles of irinotecan when administered as up-front window therapy, using a low-dose protracted intravenous schedule in high-risk, previously untreated children with metastatic rhabdomyosarcoma, (2) To describe the toxicities associated with irinotecan when administered as described in 1, (3) To describe the toxicities of a new drug pair, Vincristine and irinotecan, when given in alternating cycles with Vincristine, actinomycin D, and cyclophosphamide (VAC) during continuation therapy in patients who achieve a partial or complete response to the irinotecan window, (4) To estimate the overall and failure-free survival of children with metastatic rhabdomyosarcoma treated with irinotecan followed by VAC alone or VAC alternating with Vincristine and irinotecan plus radiotherapy, (5) To study the pharmacokinetics of irinotecan in previously untreated children with rhabdomyosarcoma who are treated on a low-dose, protracted course and who also receive Vincristine, (6) To define and compare the clinical features of patient subgroups with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation, and (7) To crudely estimate the early response rate (CR/PR), failure-free survival and survival of patients with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation as determined by as positive or negative reverse transcriptase polymerase chain reaction (RT-PCR) assay for the t(2;13) and t(1;13) on peripheral blood and marrow specimens obtained at diagnosis (see IRSG Protocol D9902 for details).

**Technical Approach:** Patients with embryonal histology greater than or equal to 10 years of age or alveolar histology (any age) who have stage 4 tumors and who do not have evidence of intracranial extension, base of skull erosion or cranial nerve palsy will be eligible to receive the two cycles of irinotecan as up-front window therapy prior to receiving the standard therapy, Vincristine, Actinomycin D, Cyclophosphamide (VAC), radiotherapy will begin at week 15. Patients with evidence of base of skull erosion or cranial nerve palsy will receive VAC alone and will begin radiotherapy at week 15. Patients with evidence of intracranial extension will receive VAC alone and begin radiotherapy at day 0.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/052

**Status:** Ongoing

**Title:** POG D9803: Randomized Study of Vincristine, Actinomycin-D, and Cyclophosphamide (VAC) versus VAC Alternating with Vincristine, Topotecan and Cyclophosphamide for Patients with Intermediate-Risk Rhabdomyosarcoma

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Feb 06

**Periodic Review:**  
N/A

**Study Objective:** (1) To compare the early response rates (i.e., CR/PR), failure-free survival (FFS) and survival of patients with intermediate risk rhabdomyosarcoma treated with surgery + RT and Vincristine, Actinomycin-D and cyclophosphamide (VAC) or the same alternating with a new combination which substitutes topotecan for actinomycin D (VAC/VTC/VAC), (2) To compare the acute and late effects of these two treatment regimens, (3) To determine the rate of second-look surgery in selected patients with bulk residual tumor at diagnosis (i.e., Clinical Group III) and the proportion of these that render the patient "tumor free" or with microscopic tumor only, (4) To determine the rate of local failure in selected patients with bulk residual tumors at diagnosis (i.e., Clinical Group III) who, following second-look resection, have response-adjusted radiotherapy dose reduction (36 Gy if in complete response or 41.4 Gy for microscopic residual disease), (5) To determine if preoperative radiotherapy followed by second-look surgery for selected patients with bulk residual disease (i.e., Clinical Group III) who respond poorly to induction chemotherapy is feasible, (6) To define and compare the clinical features of patient subgroups with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation, and (7) To crudely estimate the early response rate (CR/PR), failure-free survival and survival of patients with alveolar rhabdomyosarcoma whose tumors carry the t(2;13), t(1;13) or neither translocation as determined by a positive or negative reverse transcriptase polymerase chain reaction (RT-PCR) assay for the t(2;13) and t(1;13) on peripheral blood and marrow specimens obtained at diagnosis (see IRSG Protocol D9902 for details).

**Technical Approach:** This study will introduce topotecan to the standard therapy for intermediate risk rhabdomyosarcoma, surgery + RT and Vincristine, Actinomycin D, and Cyclophosphamide (VAC). This randomized study will compare two chemotherapy regimens, VAC versus VAC alternating with Vincristine/Topotecan/Cyclophosphamide (VTC) cycles.

**Progress:** No patients enrolled in this study during FY 00 at MAMC, however a patient transfer from Seattle, Washington is pending.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/049      **Status:** Ongoing

**Title:** POG D9902: A Group Wide Protocol for Collecting and Banking Pediatric Cancer Research Specimens. An Intergroup Rhabdomyosarcoma Study Group Protocol

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Feb 10

**Periodic Review:**  
N/A

**Study Objective:** (1) To facilitate the collection of human tissue and other biologic specimens (blood, bone marrow) from Intergroup Rhabdomyosarcoma Study Group (IRSG) investigators, (2) To provide a repository for long-term storage of tissue and other biologic specimens (blood, bone marrow) collected by IRSG investigators (referred to as the Bank), and (3) To make available, through the IRSG/Cooperative Human Tissue Network, these materials for approved projects by laboratory-based investigators.

**Technical Approach:** At the time of initial diagnosis of rhabdomyosarcoma or undifferentiated sarcoma (or at re-excision of the primary tumor, if it occurs prior to the start of chemotherapy), surgical tissue, bone marrow and blood that are no longer needed for diagnosis will be prepared and shipped to the Pediatric Cooperative Human Tissue Network (CHTN) for Banking and Distribution.

**Progress:** No patients were enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/050

**Status:** Ongoing

**Title:** POG P9754: Protocol for Patients with Newly-Diagnosed Non-Metastatic Osteosarcoma, A POG/CCG Pilot Intergroup Study

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Feb 06

**Periodic Review:**  
N/A

**Study Objective:** (1) To sequentially perform three pilot studies of dose intensified therapy for osteosarcoma: a) doxorubicin dose intensification, b) doxorubicin dose intensification with ifosfamide, c) alkylator intensification. One of these therapies will be used in a randomized study whose objectives will be: (1.1.) To determine whether postoperative dose intensification can improve outcome for standard responders to preoperative chemotherapy, (1.2.) To determine whether the use of dexrazoxane (DXR) cardioprotection during a standard preoperative induction regimen affects histologic response, (2) To pilot a standard preoperative chemotherapy regimen administered with dexrazoxane (DXR) cardioprotection for all newly diagnosed patients with non-metastatic osteosarcoma, (2.1.) To test whether DXR can be safely used with doxorubicin in combination with cisplatin (pilot 1) or cisplatin/ifosfamide (pilots 2,3), (2.2.) To ascertain that the cytotoxicity as measured by tumor necrosis at definitive surgery is not compromised by the used of DXR compared to historic control, (3) To assess the feasibility of administering 600 mg/m<sup>2</sup> of doxorubicin with DXR cardioprotection (pilot 1,2) or high dose ifosfamide the etoposide (pilot 3) to standard risk patients who are also being treated with methotrexate and cisplatin (and ifosfamide in pilots 2,3), (4) To evaluate the feasibility of obtaining tumor tissue for analysis of biologic factors in osteosarcoma in conjunction with P9851, and (5) To evaluate the feasibility of assessing musculoskeletal, cardiac, renal and gonadal status after the completion of therapy.

**Technical Approach:** Two courses of standard chemotherapy will be given prior to surgery, limiting intensification to the population at greatest risk. The cohort with a good response to therapy will continue with non-intensified chemotherapy. For the purposes of this study, good responders will have greater than or equal to 98% necrosis in the tumor specimen resected at definitive surgery. The companion biology protocol POG P9851 will accompany this study.

**Progress:** No patients were enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/018	<b>Status:</b> Ongoing
<b>Title:</b> POG P9761: Phase II Trial of Irinotecan in Children with Refractory Solid Tumors, A Pediatric Oncology Group/Children's Cancer Group Study		
<b>Principal Investigator:</b> LTC Kelly J. Faucette, MC		
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert G. Irwin, MC		
<b>Start Date:</b> 11/19/1999	<b>Est. Completion Date:</b> Nov 04	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To determine the efficacy of irinotecan in the treatment of children with refractory neuroblastoma, sarcomas of soft tissue or bone, other solid tumors, or brain tumors, (2) to further evaluate the toxicity of irinotecan when given daily for 5 days, repeated every 21 days, and (3) to further evaluate the pharmacokinetics/pharmacodynamics of irinotecan and its metabolites SN-38, SN 38G, and APC, using a limited sampling strategy.

**Technical Approach:** Irinotecan appears to be one of the most active topoisomerase I inhibitors that is clinically available and therefore deserves further evaluation in children with recurrent CNS or solid tumors. Although the optimal schedule for irinotecan is not yet known, antitumor activity has been observed on all schedules of administration. Pharmacokinetic studies, an integral component of this trial will be done to determine if there are correlates with PK parameters and toxicity or response.

**Progress:** One patient was enrolled in this study in FY00 at MAMC. No adverse events have been reported.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/048

**Status:** Ongoing

**Title:** POG P9851: Osteosarcoma Biology Protocol, Companion to Intergroup Therapeutic Studies

**Principal Investigator:** LTC Kelly J. Faucette, MC

**Department:** POG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Robert G. Irwin, MC

**Start Date:**  
2/22/2000

**Est. Completion Date:**  
Feb 10

**Periodic Review:**  
N/A

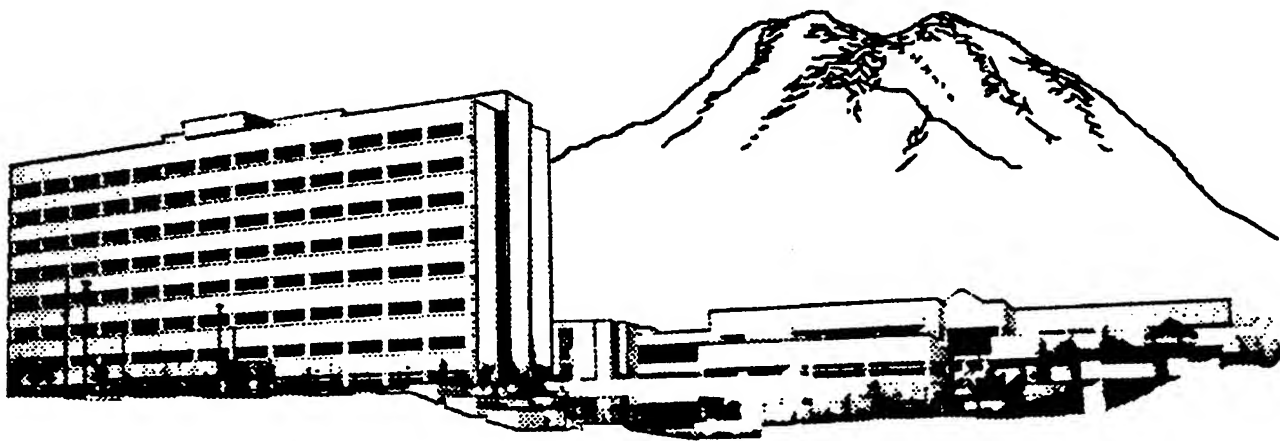
**Study Objective:** (1) To increase our understanding of the basic biology of these tumors, with a distinct possibility that new therapeutic targets may be uncovered. Examples of this type are ErbB-2 and methotrexate resistance factors, (2) To develop a set of biologic prognostic indicators which can be measured at diagnosis and which will be predictive of response and outcome in osteosarcoma. These could then be used in subsequent treatment programs to determine therapy, avoiding excessive toxicity to good risk patients and reserving alternative, more intensive therapy for those at standard risk. Examples include loss of heterozygosity at Rb and MDR, (3) To determine the feasibility of various assays and to develop a reliable mechanism of distributing osteosarcoma samples to various intergroup investigators, with centralized reporting of laboratory results and adequate quality control.

**Technical Approach:** At the time of biopsy or surgery (definitive or recurrence), tumor tissue that is not needed for diagnosis will be processed and forwarded to the Cooperative Human Tissue Network (CHTN) for distribution. Specimens will include: tumor tissue (Formalin-fixed or formalin-fixed paraffin embedded block or 30 unstained slides; blood samples (heparinized (10 ml), serum (14 ml)).

Assays being performed:

MDR Immunohistochemistry (University of Rochester)  
MDR Functional Assays/MRP (Memorial Sloan-Kettering)  
Methotrexate Transport & Metab (Memorial Sloan-Kettering)  
Topoisomerase II (Yale University)  
Bcl-2/Bax (Yale University)  
Rb/p53 (Fels Institute)  
ErbB-2 (Memorial Sloan-Kettering)  
MDM2 (Memorial Sloan-Kettering)  
p16/p21 (Hospital for Sick Children)  
LOH at 3q,18q (Fels Institute)  
sis,gli,fos (Yale University)  
SV40 (University of Colorado)  
myc,RAS (Memorial Sloan-Kettering)  
metalloproteinase (Yale University)  
c-met/HGF (Yale University)  
IGF-I/IGF-IR (University of Maryland)  
Telomerase (St. Jude Children's)  
Ploidy (Dana Farber)

**Progress:** No patients were enrolled in this study in FY00 at MAMC.



## Detail Summary Sheets

Southwest Oncology Group

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 83/056

**Status:** Ongoing

**Title:** SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC James E. Congdon, MC; COL Friedrich H. Stutz, MC; COL Irwin B. Dabe, MC; MAJ Timothy J. O'Rourke, MC; MAJ Alfred H. Chan, MC; MAJ Thomas M. Baker, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
3/18/1983

**Est. Completion Date:**  
Feb 85

**Periodic Review:**  
2/22/2000

**Study Objective:** To assess the impact of short-term intensive chemotherapy with CMFP to prevent disease recurrence and prolong survival in node negative patients with any size estrogen receptor negative tumors and node negative patients with estrogen receptor positive tumors whose pathological size is >3 cm; to assess the impact of surgical procedure, estrogen receptor status, menopausal status and tumor size; to develop guidelines referable to histopathological features of node negative tumors which are reproducible and to assess their prognostic impact for disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).

**Technical Approach:** Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cm in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

**Progress:** This study closed to patient entry 15 May 88. Twelve patients were enrolled in previous years. Three have died and nine continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 85/073      **Status:** Terminated

**Title:** SWOG 8590: Phase III Study to Determine the Effect of Combining Chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell Carcinoma of the Head and Neck, Phase III Intergroup

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Thomas M. Baker, MC; COL Friedrich H. Stutz, MC; COL Irwin B. Dabe, MC; COL William J. Gernon, MC; MAJ Timothy J. O'Rourke, MC; MAJ Michael D. Stone, MC; CPT David R. Bryson, MC; LTC Donald B. Blakeslee, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
6/28/1985

**Est. Completion Date:**  
May 87

**Periodic Review:**  
N/A

**Study Objective:** To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

**Technical Approach:** After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cisplatinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

**Progress:** This study has been terminated at MAMC. Three patients were entered in previous years. One patient is deceased and two patients will continue to be followed under SWOG 9808.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/119

**Status:** Ongoing

**Title:** SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** COL John N. Wettlaufer, MC; COL John C. Norbeck, MC; LTC Kurt L. Hansberry, MC; CPT Timothy O. Taylor, MC; CPT Michael D. Bagg, MC; CPT Bradley F. Schwartz, MC; MAJ J. Brantley Thrasher, MC; LTC Luke M. Stapleton, MC; LTC Kenneth A. Bertram, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Raymond S. Lance, MC

**Start Date:**  
6/3/1994

**Est. Completion Date:**  
Jun 98

**Periodic Review:**  
5/23/2000

**Study Objective:** 1) To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3N0M0) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. 2) To assess the qualitative and quantitative toxicities of patients with pathologic Stage C (T3N0M0) carcinoma of the prostate when treated with external beam radiotherapy.

**Technical Approach:** Patients who have undergone radical prostatectomy and pelvic lymphadenectomy for clinical Stage A or B disease with a histologically proven diagnosis of pathologic Stage C (T3N0M0) carcinoma of the prostate will be randomized to receive either postoperative adjuvant radiation therapy (ARM I) or no adjuvant therapy (ARM II). The studies primary objective is to determine whether adjuvant radiation therapy has an effect on local control of the cancer and cancer-specific survival.

**Progress:** This study was closed to patient entry 17 Jan 97. One patient was enrolled at MAMC and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 88/066                      **Status:** Ongoing

**Title:** SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG    **Facility:** MAMC

**Associate Investigator(s):** COL Irwin B. Dabe, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
7/15/1988

**Est. Completion Date:**  
Jun 91

**Periodic Review:**  
6/27/2000

**Study Objective:** To compare the effectiveness of the MOPP/ABV hybrid with sequential MOPP-->ABVD in patients with advanced or recurrent Hodgkin's disease and to determine which regimen is superior with respect to the following parameters: complete response rate, duration of complete response, freedom from progression, and survival.

**Technical Approach:** Patients must have histologic confirmation of Hodgkin's disease with no prior chemotherapy. Patients will be stratified according to age, prior radiotherapy, bulky disease, and performance status. They will then be randomized to MOPP repeated every 28 days for 6 cycles (Arm I) or to MOPP/ABV Hybrid repeated every 28 days for six cycles (Arm II). Patients on Arm I with a complete response will go on to ABVD repeated every 35 days for three cycles. Those with partial response will receive two MOPP cycles and then go on to ABVD for three cycles. Those with no change will go off study. Those patients on Arm II with complete response will receive two more cycles of MOPP/ABV. Those with partial response will continue MOPP/ABV to complete response or until a maximum of 12 cycles. Those with no change will be taken off study. MOPP: Nitrogen mustard, 6 mg/m<sup>2</sup> IV, days 1 and 8, Vincristine, 1.4 mg/m<sup>2</sup> IV, days 1 and 8, Procarbazine, 100 mg/m<sup>2</sup> PO per day x 14 days, Prednisone 40 mg/m<sup>2</sup> PO per day x 14 days. ABVD: Adriamycin, 25 mg/m<sup>2</sup> IV, days 1 and 15, Bleomycin, 10 units/m<sup>2</sup> IV, days 1 and 15, Vinblastine, 6 mg/m<sup>2</sup> IV days 1 and 15, DTIC, 375 mg/m<sup>2</sup> IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m<sup>2</sup> IV, day 8; bleomycin, 10 units/m<sup>2</sup> IV day 8; and vinblastine, 6 mg/m<sup>2</sup> IV, day 8.

**Progress:** This study was closed to patient entry 1 Aug 89. One patient was enrolled at MAMC (FY88) and continues to be followed.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 89/080

Status: Ongoing

**Title:** SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast Cancer Having Involved Axillary Nodes and Positive Hormone Receptors

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
9/15/1989

**Est. Completion Date:**  
Sep 99

**Periodic Review:**  
8/22/2000

**Study Objective:** To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

**Technical Approach:** Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/ or the other must be positive by the institutional laboratory standards of >10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR(ER positive); time from surgery to randomization (<6 vs >6 weeks). Patients will be randomized to one of three treatment arms: Arm I: Tamoxifen x 5 years, Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years, Arm III: Intermittent CAF x 6 courses with concurrent Tamoxifen x 5 years.

**Progress:** This study closed to patient entry 1 Aug 95. Seven patients have been entered in this study at MAMC. One patient died in FY 96, 6 patients continue to be followed.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 91/087	Status: Ongoing
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**Title:** SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Howard Davidson, MC; LTC Luke M. Stapleton, MC; MAJ Patrick L. Gomez, MC; MAJ Everardo E. Cobos Jr., MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; MAJ James S. D. Hu, MC; MAJ Paul C. Sowray, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
8/2/1991

**Est. Completion Date:**  
Aug 95

**Periodic Review:**  
7/25/2000

**Study Objective:** To acquire fresh snap-frozen lymphoma tissue to establish a central lymphoma tissue repository; to establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group; to use repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status; and to determine if pretreatment phenotype or genotype predict patient outcome with respect to complete response rate, time to progression, and survival using prospective trial designs.

**Technical Approach:** Patients will be treated according to guidelines outlined in the specific SWOG studies. Treatment decisions will not be based on findings of the Central Lymphoma Laboratory, although clinical variables will be correlated with laboratory findings. The tissue samples will be taken from the pretreatment diagnostic biopsy or rebiopsy based on clinical decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (hematoxylin and eosin) histologic section with accompanying pathology report. The H&E stained slide and report will accommodate morphologic correlation with immunologic findings. Tissue section analysis will be performed at the University of Arizona using three stage immunohistochemistry. Future molecular studies entailing hybridization studies of RNA and DNA fragments using DNA probes will be performed as outlined in future protocols.

**Progress:** This is a companion study using tissue from other SWOG protocols. Tissue has been collected on three patients. Two patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 90/027

**Status:** Ongoing

**Title:** SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor- Positive Breast Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
1/19/1990

**Est. Completion Date:**  
Dec 99

**Periodic Review:**  
1/5/2000

**Study Objective:** To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

**Technical Approach:** Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

**Progress:** This study closed to patient entry 15 Feb 94. Six patients have been enrolled at MAMC in previous years. One patient has been lost to follow-up, five are still being followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 91/067	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Howard Davidson, MC; MAJ Paul C. Sowray, MC; MAJ Everardo E. Cobos Jr., MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Patrick L. Gomez, MC; LTC Kenneth A. Bertram, MC		
<b>Start Date:</b> 6/14/1991	<b>Est. Completion Date:</b> Jun 94	<b>Periodic Review:</b> 5/23/2000

**Study Objective:** To evaluate the prognostic value of cellular DNA parameters of degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) in predicting treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck treated initially with cytotoxic therapy and to assess the correlation of DNA index and SPF with other patient clinical characteristics.

**Technical Approach:** Squamous cell cancers of the head and neck display a high degree of responsiveness to chemotherapy and/or radiotherapy, but a significant minority are exquisitely resistant to these treatment modalities. This will be a companion study to all SWOG head and neck cancer protocols utilizing chemotherapy as initial treatment and will use the patients registered on those studies. This study will use flow cytometrically determined cellular parameters, particularly cellular DNA content, to help identify prognostic outcome in this group of tumors. Specimens will be obtained at the time of biopsy for diagnosis, at completion of therapy if the tumor persists, or if a biopsy is performed to confirm a clinical complete response or document recurrence. All resected specimens will be sent for flow cytometry analysis. The degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) will be determined by flow cytometry. These measurements will be correlated with the clinical characteristics of the patient at the time of biopsy to help predict treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck.

**Progress:** Four patients have been entered in this study at MAMC in previous years. No new patients were enrolled in FY 00.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 90/029

Status: Ongoing

**Title:** SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History Follow-up Study in Low-Risk, Node Negative Patients

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
1/19/1990

**Est. Completion Date:**  
Jan 93

**Periodic Review:**  
1/5/2000

**Study Objective:** To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

**Technical Approach:** Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

**Progress:** This study was closed to patient entry 15 Jan 93. Nine patients were enrolled in previous years, one died in FY 97 and one was lost to further follow-up. The other seven patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 89/021      **Status:** Ongoing

**Title:** SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin + 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in Selected Patients with Durke's B or C Colon Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** COL Irwin B. Dabe, MC; MAJ Mark H. Kozakowski, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; MAJ Everardo E. Cobos Jr., MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
2/17/1989

**Est. Completion Date:**  
Feb 92

**Periodic Review:**  
1/25/2000

**Study Objective:** To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.

**Technical Approach:** Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years. Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/ mesenteric implants resected enbloc (yes/no); and obstruction (yes/no). RANDOMIZE TO: (1) Observation; (2) Leucovorin 20 mg/m<sup>2</sup> + 5-FU 425 mg/m<sup>2</sup>; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m<sup>2</sup> + 5-FU 600 mg/m<sup>2</sup>; Leucovorin by IV 2 hour infusion, 5-FU IV push beginning 1 hr after start of Leucovorin infusion, repeated weekly for 6 wks, followed by a 2-wk rest period, each 8-wk cycle (1 course) will be repeated for 4 courses. Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole).

**Progress:** Eighteen patients were enrolled at MAMC prior to closure to patient entry on 30 Jul 92. Seven patients have died from their disease and 11 continue to be followed.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 91/089

**Status:** Ongoing

**Title:** SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Howard Davidson, MC; MAJ Paul C. Sowray, MC; MAJ Patrick L. Gomez, MC; MAJ Everardo E. Cobos Jr., MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; MAJ James S. D. Hu, MC; LTC Luke M. Stapleton, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
8/2/1991

**Est. Completion Date:**  
Aug 95

**Periodic Review:**  
7/25/2000

**Study Objective:** To establish a central lymphoma serum repository that will serve as a resource to provide specimens for current and future scientific studies and to utilize the Southwest Oncology Group clinical data base to perform clinicopathologic correlations with the results of those studies.

**Technical Approach:** No therapy will be utilized in this study and patient treatment will not be based on this study. Patients must meet the eligibility criteria and be registered to one of the following SWOG protocols: 8516, 8809, 8736, or 8816. Ten cc's of blood will be drawn prior to protocol treatment and shipped to the SWOG Lymphoma Serum Repository at Loyola University Medical School.

**Progress:** This is a companion protocol to other SWOG protocols. Two specimens have been submitted in previous years. Those patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 90/056      **Status:** Ongoing

**Title:** SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Paul C. Sowray, MC; MAJ Mark H. Kozakowski, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Patrick L. Gomez, MC; CPT Denis Bouvier, MC; LTC Howard Davidson, MC; LTC Robert L. Sheffler, MC; LTC John A. Vaccaro, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
3/16/1990

**Est. Completion Date:**  
Mar 93

**Periodic Review:**  
2/22/2000

**Study Objective:** To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.

**Technical Approach:** Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study.

**Progress:** Prior to closure to patient entry, 1 Apr 92, two patients were enrolled at MAMC. One patient died, Jan 93, and the other patient continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/056

**Status:** Ongoing

**Title:** SWOG 9003: Fludarabine for Waldenstrom's Macroglobulinemia (WM): A Phase II Study for Untreated and Previously Treated Patients

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
3/5/1993

**Est. Completion Date:**  
Mar 98

**Periodic Review:**  
2/22/2000

**Study Objective:** 1) To estimate response rates and survival in patients with Waldenstrom's Macroglobulinemia (WM) receiving fludarabine, with stratification according to whether they have prior therapy. 2) To define prognostic factors that may relate to response, time to progression and overall survival, separately for newly diagnosed and previously treated patients. 3) To estimate the associated hematologic and non-hematologic toxicities.

**Technical Approach:** Persons with a diagnosis of WM and meeting enrollment criteria can be registered for this study. After the initial workup, to include bone marrow aspiration, those patients without symptoms and with no progression of the disease will be entered in the Observation phase. If they are symptomatic or have progression of the disease or if onset of symptoms and/or progression occurs during the Observation phase immediate Re-registration to the Treatment phase will occur. Fludarabine 30 mg/m<sup>2</sup> IV will be administered on days 1 - 5. This schedule will be repeated every 28 days for 4 cycles until the patient's condition is stable without remission, progression occurs, or the disease is stable. If the disease becomes stable without remission or progresses, treatment will be stopped. If there is complete remission, partial remission or improvement the patient will receive an additional 4 cycles of therapy or 2 cycles beyond maximum response, whichever occurs earlier.

**Progress:** The protocol was closed to patient accrual 1 Sep 98. Two patients were enrolled in FY 93 and continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 91/094		<b>Status:</b> Ongoing	
<b>Title:</b> SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary					
<b>Principal Investigator:</b> MAJ David E. McCune, MC					
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Associate Investigator(s):</b> LTC Howard Davidson, MC; MAJ Paul C. Sowray, MC; LTC Luke M. Stapleton, MC; MAJ Patrick L. Gomez, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; CPT Jennifer L. Cadiz, MC; MAJ James S. D. Hu, MC; LTC Kenneth A. Bertram, MC					
<b>Start Date:</b> 9/6/1991		<b>Est. Completion Date:</b> Aug 94		<b>Periodic Review:</b> 8/22/2000	

**Study Objective:** To compare these primary aspects of quality of life, according to treatment assignment: 1) Treatment specific symptoms 2) Physical Functioning 3) Emotional functioning. To compare three secondary quality of life variables, according to treatment assignment: 1) General symptoms 2) Global perception of quality of life 3) Social functioning.

**Technical Approach:** This is a companion to SWOG 8794. Patients will be assigned to the same treatment groups as in the companion protocol (prostatectomy followed by adjuvant radiotherapy versus prostatectomy alone) and must be able to complete a quality of life questionnaire prior to registration and randomization on SWOG-8794. Standardized instructions will be read to the patients by the nurse/data manager at each site. Additional questionnaires will be completed at week 6, 6 months, 12 months, and then yearly for the next 4 years. Quality of life profiles will be compared for the two treatment groups at different points in time: baseline, where no differences are expected six weeks, where the two treatment groups are expected to show maximum differences on some measures; six months, one year and annually for a total for five years, where the treatment means for quality of life measures are expected to come together and level off. For key continuous variables, repeated measures analyses of variance should help to make comparisons at fixed points in time and across time. For the discrete variables such as occurrence or non-occurrence of specified complications, standard methods of categorical data analysis will be employed.

**Progress:** No patients were enrolled in FY00 at MAMC. Five patients have been enrolled in previous years. Three patients have died and two patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 91/033      **Status:** Ongoing

**Title:** SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for Patients with Local Regional Disease

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Howard Davidson, MC; MAJ William A. Phillips; LTC Luke M. Stapleton, MC; MAJ Patrick L. Gomez, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; COL Joseph F. Homann, MC; COL Daniel G. Cavanaugh, MC; MAJ Everardo E. Cobos Jr., MC; MAJ Paul C. Sowray, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
2/1/1991

**Est. Completion Date:**  
Jan 94

**Periodic Review:**  
1/25/2000

**Study Objective:** To compare, using a prospective controlled randomized study design, the outcomes of therapy of surgery alone versus pre and postoperative chemotherapy and surgery for patients with local regional esophageal cancer (outcome is defined as survival and relapse pattern); to assess the toxicities of a multimodality approach to esophageal carcinoma involving systemic chemotherapy and surgery (the toxicities of surgical resection as initial therapy or following chemotherapy will be assessed as operative morbidity and mortality); to compare the local and distant control rates with the two approaches and to define the pattern of failure; and to compare the impact on overall and disease free survival of multimodality therapy with surgery alone.

**Technical Approach:** Esophageal cancer is seen in over 10,000 patients a year in the United States and only about 7% of these patients are cured as demonstrated by a five year survival. This study is designed to see whether or not giving chemotherapy will improve that survival. To be eligible patients must have histologic proof of squamous cell carcinoma of the esophagus, disease limited to the total regional area (clinical stage T1-T3, NX,MO), no prior surgery, radiation therapy, or chemotherapy, and adequate bone marrow, liver function, renal function, and pulmonary reserve. Patients must be physiologically fit for proposed chemotherapy and surgery and be greater than 18 years of age. Patients will be randomized to surgery alone, or to receive three cycles of preoperative cisplatin and 5-FU and then to undergo definitive surgery followed by two more cycles of cisplatin and 5-FU, starting two to six weeks after surgery.

**Progress:** This study was closed to patient entry 31 Dec 95. Three patients were enrolled in this study at MAMC. One patient died of progressive disease and two patients continue to be followed.

### Detail Summary Sheet

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<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/062	<b>Status:</b> Ongoing
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**Title:** SWOG 9035: Randomized Trial of Adjuvant Immunotherapy with an Allogeneic Melanoma Vaccine for Patients with Intermediate Thickness, Node Negative Malignant Melanoma, Phase III

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Richard F. Williams, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

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**Start Date:**  
1/20/1995

**Est. Completion Date:**  
Jan 99

**Periodic Review:**  
1/25/2000

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**Study Objective:** 1) To compare disease-free survival and overall survival between patients with T3NOM0 malignant melanoma who receive adjuvant immunotherapy with an allogeneic melanoma vaccine versus no adjuvant treatment. 2) To evaluate the toxicity of adjuvant immunotherapy with an allogeneic melanoma vaccine in patients with T3NOI10 malignant melanoma. 3) To explore the interaction between the patients' defined HLA types (i.e., whether they are compatible with the HLA phenotypes of the vaccine) and the vaccine treatment effectiveness in terms of disease-free survival and overall survival.

**Technical Approach:** The study is a randomized study of Interferon Alfa-2b as adjuvant immunotherapy in patients with T3NOM0 malignant melanoma following complete resection. After complete staging, including assessment of any abnormal lymph nodes by biopsy, patients will be randomized either to treatment with four cycles of intramuscular vaccine therapy or observation only and will be followed until death for recurrence.

**Progress:** This protocol closed to patient accrual, 15 Nov 96. One patient was enrolled in FY 95 and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 91/069

**Status:** Ongoing

**Title:** SWOG 9040 (CALGB-9081, INT-0014): Intergroup Rectal Adjuvant Protocol, A Phase III Study

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Everardo E. Cobos Jr., MC; MAJ Paul C. Sowray, MC; MAJ Patrick L. Gomez, MC; MAJ Rahul N. Dewan, MC; LTC Steven S. Wilson, MC; LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; LTC Howard Davidson, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
6/14/1991

**Est. Completion Date:**  
May 93

**Periodic Review:**  
5/23/2000

**Study Objective:** To determine the relative efficacy of: 5-FU; 5-FU plus leucovorin; 5-FU plus levamisole; and 5-FU plus leucovorin and levamisole when combined with pelvic radiation therapy in the treatment of Stages B-2 and C (TNM Stage II and III) rectal cancer. End points used will include local recurrence rates, probability of distant metastases, disease free survival rates, and overall survival.

**Technical Approach:** This will be a 4-armed study with the same radiation therapy program in all arms, but with varying drug regimens as listed in the objective. 5-FU with radiation therapy will comprise the control arm of the study. Patients will be randomized to treatment arms and they will be stratified by type of operation (abdominal perineal or anterior resection); nodal involvement (none, 1-3, or >3); and invasion through bowel wall or into adjacent organs (none, through muscularis propria, or adherence to or invasion of adjacent organs or structures). Each drug regimen will be given alone on days 1-5 and 29-33, followed by radiation therapy (five weeks) with concomitant chemotherapy on days 57-60 and 85-88. The chemotherapy regimen will then be repeated beginning 28 days after the completion of radiation therapy on days 1-5 and 29-33. If evidence of recurrence is obtained, protocol treatment will be discontinued and the patient followed until death. In the absence of recurrent disease, follow-up observations will be continued for a minimum of 5 years after surgery.

**Progress:** This study was closed to patient entry on 22 Nov 92. Three patients were enrolled in previous years and continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/104

**Status:** Ongoing

**Title:** SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC

**Start Date:**  
5/6/1994

**Est. Completion Date:**  
May 98

**Periodic Review:**  
4/25/2000

**Study Objective:** This is a preliminary effort towards the long-term research goal of determining whether calcium, as a nutritional supplement, can prevent colorectal adenomas and new primary carcinomas in surgically treated colorectal carcinoma (CRC) patients.

**Technical Approach:** Patients with previously resected colon cancer, Stages 0, I, or II or rectal carcinomas, Stages 0, I are eligible to participate in this study. During the 3 month Run In period, patients will be placed on placebo 3 tablet a day. After successful completion of the Run In (patients must have taken > 80% of tablets) patients will be randomized to regimen A (3 - 600 mg tablets of calcium carbonate daily for 5 years) or regimen b (3 placebo tablets daily for 5 years). The pills will be provided to the patients every three months for the first two years and every six months for the next three years. Patients will be monitored for compliance, hypercalcemia, renal toxicity and gastrointestinal or hepatic toxicity. Endpoint is the efficacy of supplemental oral calcium in reducing recurrence of adenomas or second primary carcinomas.

**Progress:** This protocol closed to patient accrual 22 Nov 98. Sixteen patients have been enrolled and continue to be followed.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/096

**Status:** Ongoing

**Title:** SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-Fluorouracil, in Patients with Unresectable Squamous Cell Carcinoma of the Head and Neck

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC

**Start Date:**  
5/16/1997

**Est. Completion Date:**  
Apr 00

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) To compare the effectiveness of standard radiation therapy alone to radiation therapy and simultaneous chemotherapy with cisplatin to split-course radiation therapy with cisplatin and 5-fluorouracil infusion in patients with unresectable Stage III and IV squamous cell carcinoma of the head and neck. Endpoints will include complete response rate, time to treatment failure, and overall survival. 2) To compare the relative toxicities of these treatment arms, in this patient population. 3) To compare patterns of relapse or treatment failure among these regimens. 4) To further assess the role, timing, and success of surgery in patients achieving a response to non-operative therapy.

**Technical Approach:** Unresectable Squamous Cell Carcinoma has a dismal prognosis with 3 year survivals in the 25% range. Several studies have shown that adding chemotherapy to radiation therapy may improve response rates and may allow some patients to get surgery after therapy. There are two approaches to adding chemotherapy to radiation therapy. One way is to give concurrent therapy with Cisplatin alone with combined continuous radiation therapy (Al Sarraf regimen) or to give combination Cisplatin and 5-FU with split course (Adelstein Regimen). These two regimens have met with some success in single ARM Phase II studies and have resulted in some patients having subsequent surgeries translating into longer survivals. It is thus the aim of this study to evaluate efficacy of three different regimens with continuous radiation therapy alone serving as the third ARM. Toxicities from these regimens are reasonable.

**Progress:** This study closed to patient entry 29 Nov 99. Two patients have been enrolled in this study at MAMC and continue to be followed. No patients were enrolled in FY 00.

### Detail Summary Sheet

Date: 29 Sep 00

Number: 93/032

Status: Ongoing

**Title:** SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
12/4/1992

**Est. Completion Date:**  
Nov 95

**Periodic Review:**  
1/25/2000

**Study Objective:** To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

**Technical Approach:** Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m<sup>2</sup> PO X 14 days, doxorubicin 30 mg/m<sup>2</sup> IV days 1 & 8, and fluorouracil 500 mg/m<sup>2</sup> IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m<sup>2</sup>/96 hr and ThioTEPA 800 mg/m<sup>2</sup>/96 hr (4 days), will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m<sup>2</sup>/d. Treatment will continue until the patient has achieved an absolute neutrophil count (ANC) of  $\geq 1000$  cells/ul on 3 consecutive days or a planned duration of 28 days of treatment.

Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Patients will be taken off-study if there is development of metastatic disease at any time while therapy is ongoing.

Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death)

At measured times during the study a Breast Chemotherapy Questionnaire (BCQ) will be completed to separately document the changes in psychosocial function that occur on the two regimens. Not all subjects will complete the questionnaire at all time points, but if at least 150 per arm have complete data, the width of a 95% confidence interval on the mean change in scores would be about  $\pm 0.09$

The BCG will also be used to make comparisons between regimens. A 2 degree of freedom test based on the difference of the means of the 36 week evaluation and the difference of the means of the 52 week evaluation will be used. Then using the variance information given above, the variance of the difference of means at either time should have a variance of about 0.0099, and the covariance between the two times should be about 0.0079. If there is a constant difference in the scores, then the distribution of the test statistic would be approximately noncentral chi-square with 2 degrees of freedom and centrality paraments  $113*d*d$ . For a 5% level test, this gives a power of 82% for detecting a difference of  $d = 0.3$ .

**Progress:** This protocol closed to patient accrual 3 Aug 98. One patient was enrolled in this study at MAMC and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 94/097      **Status:** Ongoing

**Title:** SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG      **Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
5/6/1994

**Est. Completion Date:**  
Sep 01

**Periodic Review:**  
4/25/2000

**Study Objective:** The main objective of this study is to compare progression-free and overall survivals of clinically stage (non-laparotomized) patients with early stage (IA, IIA), good-prognosis Hodgkin's Disease treated with either standard subtotal nodal irradiation or with short-course chemotherapy plus standard irradiation. In addition, the study will attempt to identify subgroups of patients who may do better with one approach or the other, and to follow patients for long-term toxicities associated with either regimen.

**Technical Approach:** Patients will be clinically staged by standard methods and then, if they appear to have localized, good-prognosis disease, they will be randomized to receive either standard radiotherapy to mantle and para-aortic fields (subtotal nodal irradiation) or three cycles (6 doses) of chemotherapy followed by the same radiotherapy. Management of both patient groups will be identical apart from the chemotherapy.

**Progress:** This study closed to patient entry, 24 Apr 00, when the accrual goal was reached. Two patients were enrolled in this study, both in FY 94. One patient died in FY 97 and the other patient continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/042

**Status:** Completed

**Title:** SWOG 9201 (RTOG 91-11): Phase III Trial to Preserve the Larynx: Induction Chemotherapy and Radiation Therapy versus Concomitant Chemotherapy and Radiation Therapy Versus Radiation

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; MAJ Mark E. Shaves, MC; CPT Brent L. Kane, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
12/19/1996

**Est. Completion Date:**  
Nov 00

**Periodic Review:**  
11/19/1999

**Study Objective:** The normal treatment of cancer of the throat is surgery with removal of the voice box. The purpose of this study is to try to preserve the larynx by using a non-surgical treatment. Three treatments will be compared: 1) chemotherapy followed by radiation, or 2) chemotherapy given at the same time as radiation, or 3) radiation alone.

**Technical Approach:** Treatment 1: Cisplatin and 5-FU will be given twice 3 weeks apart. Treatment 2: Cisplatin will be given once every 21 days (for three doses on Days 1, 22, and 43) during radiation which is given once a day, 5 days a week for 7 weeks. Radiation can be given on an outpatient basis. Cisplatin is given into the vein over 20-30 minutes. 5-FU is given into the vein by continuous infusion over 120 hours following cisplatin administration in Treatment 1.

**Progress:** This study was permanently closed 31 May 00, as accrual goal had been met. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/097

**Status:** Ongoing

**Title:** SWOG 9205: Central Prostate Cancer Serum Repository Protocol

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Robert L. Sheffler, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Timothy P. Rearden, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
5/7/1993

**Est. Completion Date:**  
Mar 95

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2) To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.

**Technical Approach:** This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols

All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20°C. Samples will be frozen and shipped to the Serum Bank Coordinator.

**Progress:** No patients were enrolled in FY00 at MAMC. Two patients enrolled in this serum study in FY 97, and two enrolled in previous years, for a total enrollment of 4. Three patients have died; one patient continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/115

**Status:** Completed

**Title:** SWOG 9208: Health Status and Quality of Life in Patients With Early Stage Hodgkin's Disease: A Companion Study to SWOG 9133

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ James S. D. Hu, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC

**Start Date:**  
6/3/1994

**Est. Completion Date:**  
Jun 98

**Periodic Review:**  
9/28/1999

**Study Objective:** 1) To evaluate prospectively the health status and quality of life (QOL) of early stage Hodgkin's Disease patients receiving either subtotal nodal irradiation or short course chemotherapy plus subtotal nodal irradiation. 2) To describe the short-term, acute effects of two treatments for early stage Hodgkin's Disease patients on patient report of symptoms and on patient QOL. 3) To evaluate the intermediate and long-term effects of two treatments for early stage Hodgkin's Disease patients on patient QOL over five years.

**Technical Approach:** Patients enrolled in the companion protocol, SWOG-9133, will be asked to complete questionnaires before registration into this study, at 6 months; and annually for seven years. These questionnaires seek to identify and quantitate those differences pertaining to quality of life issues that the added chemotherapy may have in early stage Hodgkin's disease patients.

**Progress:** This study closed to patient entry 24 Apr 00, when the treating protocol closed. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 94/010	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup		
<b>Principal Investigator:</b> MAJ Raymond S. Lance, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Raymond A. Costabile, MC; MAJ J. Brantley Thrasher, MC		
<b>Start Date:</b> 10/1/1993	<b>Est. Completion Date:</b> Nov 03	<b>Periodic Review:</b> 9/28/1999

**Study Objective:** The primary objective of this trial will be to determine if finasteride can reduce the development of prostatic cancer in males 55 years and older.

**Technical Approach:** Men who have attained 55 years of age have never been diagnosed as having prostatic cancer will be randomized to receive Finasteride 5 mg or Matched Placebo PO daily for 7 years. Patients will be followed with clinic visits at 6 months, 1 year and then annually. Annual laboratory screening will include PSA. Triggers are in place to initiate prostatic biopsies. The final endpoint is biopsy proven presence/absence of carcinoma of the prostate after seven years.

**Progress:** Approximately 50 patients have been enrolled in this study and continue to receive treatment. The protocol was closed to patient entry 1 Jan 97.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/136

**Status:** Ongoing

**Title:** SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; LTC Robert D. Vallion, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; MAJ Timothy P. Rearden, MC; CPT Diana S. Willadsen, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
7/2/1993

**Est. Completion Date:**  
Jul 98

**Periodic Review:**  
6/27/2000

**Study Objective:** To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

**Technical Approach:** Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

**Progress:** The protocol closed to patient accrual 9 Apr 97. Ten patients have been enrolled in this study. One patient was transferred to Keesler, three patients died, 6 patients continue to be followed at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 93/108      **Status:** Ongoing

**Title:** SWOG 9237: Evaluation of Topotecan in Refractory and Relapsing Multiple Myeloma

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ James S. D. Hu, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
5/7/1993

**Est. Completion Date:**  
May 98

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) To evaluate the response rate for refractory myeloma treated with topotecan; 2) To evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study; 3) To measure topoisomerase levels in multiple myeloma cells.

**Technical Approach:** Patients with proven multiple myeloma, with protein criteria present, who have received exactly one prior regimen, and have shown, in the opinion of the investigator, to have disease progression are eligible for this study. All patients will receive topotecan 1.25 mg/m<sup>2</sup> q.d. IV over 30 minutes on days 1-5 repeated q 21 days. This schedule will continue as long as patients show complete remission, partial remission or stable disease and toxicity is acceptable. Topotecan dosage can be adjusted on nadir counts of the preceding cycle

It is assumed that topotecan will be of interest if a true response rate of 20% or more is achieved in the treatment of patients with relapsed or refractory multiple myeloma.

**Progress:** This study closed to patient accrual 15 Feb 95. One patient was entered in this study in FY 93 and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 93/092

**Status:** Ongoing

**Title:** SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; CPT Jennifer L. Cadiz, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; CPT Diana S. Willadsen, MC; LTC Robert D. Vallion, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
4/2/1993

**Est. Completion Date:**  
May 95

**Periodic Review:**  
3/28/2000

**Study Objective:** 1. To acquire fresh snap-frozen lymphoma tissue from patients who relapse or have recurrent disease after being treated on Southwest Oncology Group treatment protocols. 2. To establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group. 3. To use the repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status. 4. To examine the biology of therapy failure in relationship to changes in pretreatment and post-therapy immunophenotypic data.

**Technical Approach:** Fresh frozen tissues will be acquired from relapsed patients for basic science protocols, both current and future, designed to better define the biology of relapsed non-Hodgkins's lymphoma. This is not a treatment protocol, nor will results be used to guide treatment decisions

Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (Hematoxylin and Eosin) histologic section with accompanying pathology report to The Department of Pathology at the University of Arizona in Tucson.

**Progress:** No patients have been enrolled in this study in FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/161

**Status:** Completed

**Title:** SWOG 9250 (INT-0136): Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients With Colon Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
9/21/1994

**Est. Completion Date:**  
Sep 98

**Periodic Review:**  
8/24/1999

**Study Objective:** To determine if (1) adjuvant therapy with one week of continuous 5-FU given within 24 hours of a curative colon resection followed by 12 months of 5-FU/Levamisole is effective in prolonging the disease free interval and increasing survival in patients who are treated with 5-FU/Levamisole only. Endpoints include: treatment failure - as described by recurrence of local/regional or distant metastases - and survival. (2) To establish within ECOG a Central Tissue Repository for paraffin blocks and a frozen tissue bank.

**Technical Approach:** Patients with primary colon cancer will be randomized to either receive 7 days of continuous intravenous 5-fluorouracil (5-FU) within 24 hours completion of colon surgery or not to receive any perioperative chemotherapy. The only investigational part of this protocol is the administration of chemo-therapy during the period right after subjects colon operation. The operation and the use of 5-FU/levamisole are all standard treatment.

**Progress:** This study was permanently closed 19 May 00, due to poor patient accrual. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/073

**Status:** Completed

**Title:** SWOG 9300: A Randomized Phase II Evaluation of All Trans-Retinoic Acid with Interferon-Alfa 2a or All Trans-Retinoic Acid with Hydroxyurea in Patients with Newly Diagnosed Chronic Myelogenous Leukemia in Chronic Phase

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Mark E. Robson, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC

**Start Date:**  
3/4/1994

**Est. Completion Date:**  
Mar 94

**Periodic Review:**  
2/23/1999

**Study Objective:** 1). To estimate whether treatment of Chronic Myelogeneous Leukemia (CML), with all-trans retinoic acid in combination with either hydroxyurea or interferon alfa-2a is sufficiently effective based on either hematologic or cytogenetic response, to justify its investigation in phase III trials. 2). To assess the toxicities associated with all-trans retinoic acid plus hydroxyurea or itnerferon alfa-2a in chronic phase CML.

**Technical Approach:** Patients qualifying for this study will be stratified by age (< 45 vs >=45), splenomegaly (present vs absent), prior hydroxyurea (yes or no), and ANC at diagnosis (<50,000 ul). Patients will then be randomized to one of two treatment arms as follows: Arm I: ATRA and HU or Arm II: ATRA and IFN. This randomization will be dynamically balanced to assure roughly equal numbers of patients within levels of the stratifying factors

All patients in both arms will begin treatment with HU to control or keep the WBC <= 20,000/ul and platelets <=800,000/ul. All therapy will include allopurinol. Patients will receive this HUS treatment for a minimum of 21 days and a maximum of 42 days. Patients with WVA <= 20,000/ul, platelets <=800,00/ul, and no evidence of progressive splenomegaly after 21 - 42 days of HU will then bergin treatment on their assigned regimens. Patients who do not achieve a WBC <= 20,000/ul, platelets <=800,000/ul, and absence of progressive splenonegaly after 42 days will be removed from protocol treatment

Arm I patients will receive ATRA 150/mg/M2/d x 7 days followed by 7 days rest and HU 500 mg qd adjusted to maintain WBC and platelets to predefined levels

Arm II patients will receive acetaminophen 650 mg 1/2 hr before administration of IFN initiated a 3 MIU/M2/d 5 days/week escalated by 1 MIU/M2 each week to a maximum of 5 MIU/M2day/ and ATRA 150 mg/M2/d x 7 days followed by 7 days rest

Treatment regimens will continue until the onset of accelerated or blast phase or relapse from CR or PR. Bone marrow aspiration and biopsy to monitor disease status are required at 3 and 6 months and every 6 months thereafter. Serial blood and urine specimens will be obtained for laboratory analysis.

**Progress:** This study closed to patient accrual, 1 Dec 99. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 93/166      **Status:** Ongoing

**Title:** SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; MAJ Richard C. Tenglin, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
9/3/1993

**Est. Completion Date:**  
Oct 98

**Periodic Review:**  
8/22/2000

**Study Objective:** To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T4BN0-2 colon cancer and selected patients with T3N1-2 colon cancer.

**Technical Approach:** This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

**Progress:** This study was closed to patient entry 17 Dec 96. One patient was enrolled in this study at MAMC in FY 95 and continues to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/111

**Status:** Ongoing

**Title:** SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU + Leucovorin + Levamisole Prior to and Following Combined Pelvic XRT + Bolus 5-FU + Leucovorin in Patients with Rectal Cancer, Phase III Intergroup

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC

**Start Date:**  
5/6/1994

**Est. Completion Date:**  
May 98

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged venous infusion given prior to and following combined pelvic x-ray (XRT) therapy + protracted venous infusion (PVI) vs. 5-FU by bolus injection plus LV plus LEV given prior to and following combined pelvic XRT plus bolus 5-FU plus LV in the treatment of modified Aster-Coller Stages B2, B3 and C rectal cancer. This will be evaluated in terms of survival and relapse-free survival

2) To obtain descriptive information regarding relapse patterns and tolerance.

**Technical Approach:** Patients entering this study will be randomized to one of three treatment arms. Patients in all arms will receive pelvic radiotherapy. Those randomized to Arms A and B will receive concomitant 5-FU by PVI (225 mg/M2/d) during radiotherapy. Each patient will be randomly allocated to receive 5-FU +/- LV and levamisole for 2 months prior to and for 2 months following combined chemo-radiotherapy. Patients will be randomized to chemotherapy prior to and following chemo-radiotherapy as follows:

- a. Arm A: bolus IV injection of 5-FU alone
- b. Arm B: protracted venous infusion of 5-FU alone
- c. Arm C: bolus 5-FU + LV + levamisole before and after pelvic radio therapy; bolus 5-FU + LV during pelvic radiotherapy

After completion of all therapy patients will be followed every 4 months X 2 years, then every 6 months X 4 years.

**Progress:** This study closed to patient entry Sep 00. Four patients have been enrolled in this study at MAMC. One patient is on active treatment, one patient died in FY 96 and two patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 94/170      **Status:** Ongoing

**Title:** SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast Cancer Patients with 0-3 Positive Nodes

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
9/21/1994

**Est. Completion Date:**  
Sep 98

**Periodic Review:**  
8/22/2000

**Study Objective:** 1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide. 2) To obtain tumor tissue for biologic studies.

**Technical Approach:** Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.

**Progress:** The protocol was closed to patient entry 1 May 97. One patient has been enrolled in this study at MAMC and continues to be followed.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/107

**Status:** Completed

**Title:** SWOG 9321: Standard Dose Versus Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma, Phase III

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ James S. D. Hu, MC; MAJ Patrick L. Gomez, MC; MAJ Timothy P. Rearden, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC

**Start Date:**  
5/6/1994

**Est. Completion Date:**  
May 98

**Periodic Review:**  
4/25/2000

**Study Objective:** 1. To perform a randomized trial, in newly diagnosed patients with symptomatic multiple myeloma (MM), of standard therapy versus myeloablative therapy, in order to examine whether the greater tumor cytoreduction effected by intensive therapy and manifested by higher incidence of complete remission translates into extended overall survival and progression-free survival

2. To randomize responding patients with  $\geq 75\%$  tumor cytoreduction to interferon-alpha 2b (IFN) versus no maintenance in order to evaluate the role of IFN in MM.

**Technical Approach:** Symptomatic patients of all stages of multiple myeloma with reasonable performance status will be randomized to high dose chemotherapy with autologous bone marrow transplant or standard VBMCP combination chemotherapy after induction VAD therapy. A required peripheral stem cell harvest will be done for those randomized to the ABMT arm for future high dose therapy if failure occurs. This will be an option for those randomized to the standard arm. Those patients that have an HLA compatible sibling donor will be eligible for allogeneic BMT. A second randomization will be done for those with continued greater than 75 percent regression of disease in the ABMT or standard chemotherapy arm while those receiving allo-BMT will be continued on GVHD prophylaxis.

**Progress:** This study closed to patient enrollment 1 Oct 00. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 94/058                      **Status:** Ongoing

**Title:** SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; MAJ Patrick L. Gomez, MC; MAJ Mark E. Robson, MC; LTC Robert B. Ellis, MC; LTC Kenneth A. Bertram, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC

**Start Date:**  
2/4/1994

**Est. Completion Date:**  
Nov 03

**Periodic Review:**  
1/25/2000

**Study Objective:** 1) To evaluate the reproducibility of a combined histopathologic grading system of breast cancer. 2) To evaluate the ability of the grading system to predict time to treatment relapse (TTR) and survival. 3) To use multivariate analyses to evaluate the prognostic importance of the grading data relative to the other clinical and biological factors determined as part of SWOG 8294.

**Technical Approach:** This is a pathology study utilizing the patient set from SWOG 8294. Patients reviewed as part of that study (where cases with adequate specimens for flow cytometry were evaluated and provisionally graded) will be registered to this study. Slides will be reviewed by three investigators and cases will be grouped into 3 prognostic categories. The power calculation for testing the association of this grading system with survival will be based on the "2 degree of freedom" logrank test. The Cox proportional hazards model will also be used in the analysis to adjust the comparisons for effects of other factors.

**Progress:** This study closed to patient accrual 5 Oct 95. Seven patients were enrolled in this study in FY 94. One patient died, and six patients continue to be followed on the treatment protocol.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/121

**Status:** Ongoing

**Title:** SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell Lung Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** COL Daniel G. Cavanaugh, MC; COL Walter G. Graves, MC; LTC Maceo Braxton Jr, MC; LTC Blaine R. Heric, MC; MAJ Rahul N. Dewan, MC; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; LTC Robert D. Vallion, MC; MAJ Patrick L. Gomez, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
6/3/1994

**Est. Completion Date:**  
Jun 98

**Periodic Review:**  
5/23/2000

**Study Objective:** 1) Assess whether concurrent chemotherapy and radiotherapy followed by surgical resection results in a significant improvement in progression-free, median, and long-term (2 year, 5 year)s survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2-positive) non-small cell lung cancer

2) Evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastases

3) To obtain exploratory descriptive information on the relationship of tobacco use, alcohol use and dietary patterns on toxicity and outcomes in males and females.

**Technical Approach:** Patients with biopsy-proven Stage IIIa Non-Small Cell carcinoma will be randomized to one of two arms. Arm I and II patients will receive Induction Radiotherapy (45 Gy + concurrent induction chemotherapy (CT) of Cisplatin 50 mg/M2 IVPB days 1, 8, 29, 36 and VP-16 50 mg/M2 IVPB, days 1-5, 29-33. Arm I patients will be re-evaluated 2-4 weeks after completion of induction and Arm II will be re-evaluated 7 days before completion of induction. All patients, after re-evaluation, will proceed to Registration 2. If there is no evidence of local progression or distant metastases patients will be assigned options 3 or 4 (Arm I) or option 5 (Arm II). Option 3 consists of surgery plus 2 additional cycles CT starting 4-6 weeks postoperatively, Option 4 of 2 additional cycles CT at least 3 weeks after cycle 2 and Option 5 of continuing RT with no break and beginning 2 additional cycles of CT 3 weeks after cycle 2, day 8. RT boost field will be planned by CT scan. The major endpoints will be median, 2-year and 5- year progression-free and overall survival. Evaluation of patterns of relapse is a secondary endpoint.

**Progress:** One patient enrolled in this study in FY 00 at MAMC. Two patients enrolled in this study in FY 95; however, both patients are now deceased.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 95/003

**Status:** Ongoing

**Title:** SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
10/21/1994

**Est. Completion Date:**  
Oct 98

**Periodic Review:**  
9/26/1999

**Study Objective:** To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

**Technical Approach:** Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

**Progress:** This study closed to patient accrual 10 Sep 96. One patient was enrolled in FY 96 and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/093	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; CPT Diana S. Willadsen, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC		
<b>Start Date:</b> 3/17/1995	<b>Est. Completion Date:</b> Feb 99	<b>Periodic Review:</b> 2/22/2000

**Study Objective:** 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe ( $\geq$  grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.

**Technical Approach:** This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizable subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. Patients whose tumors progress on chemotherapy will proceed to RT immediately. There will be a central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy  $\pm$  PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess cognitive ability. Assessment of differences in quantitative survival will be performed between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA.

**Progress:** One patient enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 94/163

**Status:** Ongoing

**Title:** SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; LTC Robert B. Ellis, MC; MAJ Timothy P. Rearden, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
9/21/1994

**Est. Completion Date:**  
Sep 98

**Periodic Review:**  
8/22/2000

**Study Objective:** To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

**Technical Approach:** Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

**Progress:** This protocol closed to patient accrual 15 Apr 97. Nine patients were enrolled at MAMC. Three patients have died, the other six continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 95/094	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9415: Phase III Randomized Trial of 5-FU/Leucovorin/Levamisole versus 5-FU Continuous Infusion Levamisole as Adjuvant Therapy for High -Risk Resectable Colon Cancer, Intergroup		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Luke M. Stapleton, MC; LTC Howard Davidson, MC; MAJ Timothy P. Rearden, MC; LTC Robert B. Ellis, MC; MAJ James S. D. Hu, MC; LTC Robert D. Vallion, MC; CPT Diana S. Willadsen, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; LTC Kenneth A. Bertram, MC		
<b>Start Date:</b> 3/17/1995	<b>Est. Completion Date:</b> Feb 99	<b>Periodic Review:</b> 2/22/2000

**Study Objective:** To compare the effectiveness of bolus 5-FU, leucovorin, levamisole versus continuous infusion 5-FU, levamisole as adjuvant therapy for patients with Stage B2, C1 or C2 colon cancer. This will be measured in terms of overall survival. Disease-free survival will be a secondary endpoint.

**Technical Approach:** This trial is an intergroup trial involving the Southwest Oncology Group, Eastern Cooperative Oncology Group and the Cancer and Leukemia Group B. Based on previous experience with accrual to INT-0089, and assuming that roughly 1/3 of patients eligible for that study will be entered we anticipate an annual accrual of approximately 600 patients having curative resection of B2, C1, or C2 colon cancer. The primary objective of this study is to compare the survival in patients with high risk resectable colon surgery treated in an adjuvant setting with either 5-FU, leucovorin, levamisole or continuous infusion 5-FU, levamisole. The continuous infusion arm would be judged superior if the true increase in survival is 35%. A secondary endpoint will be disease-free survival. The dose of continuous infusion 5-FU selected for this study of 250 mg/m<sup>2</sup>/d is currently being piloted at an individual institution, and is lower than the common dose of 300 mg/m<sup>2</sup>/d, which required dose reductions in a previous pilot. In order to verify the appropriateness of this dose in the intergroup setting, we will evaluate toxicity and compliance in the first 40 patients randomized to the continuous infusion arm. Should the frequency of dose reductions or toxicities warrant concern, the study may be amended or temporarily closed while the continuous infusion therapy is reassessed.

**Progress:** This study closed to patient entry 15 Dec 99. One patient was enrolled in FY 97 at MAMC and continues to be followed. No patients were enrolled in FY 00.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 97/134      **Status:** Ongoing

**Title:** SWOG 9419: Tumor Tissue Biopsy for Thymidylate Synthase Expression in Patients with Colorectal Cancer, Ancillary

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC

**Start Date:**  
8/15/1997

**Est. Completion Date:**  
Apr 01

**Periodic Review:**  
7/25/2000

**Study Objective:** 1) To measure thymidylate synthase (TS) expression by polymerase chain reaction in tumor biopsies prior to initiation of fluorinated pyrimidine based therapy in patients with disseminated colorectal cancer and correlate tumor response with level of TS expression; 2) To correlate TS expression in tumor tissue obtained during a potentially curative resection and disease-free survival in patients with Stage II and III large bowel cancer prior to receiving adjuvant therapy with 5-FU based regimen on targeted Southwest Oncology Group trials.

**Technical Approach:** Tissue samples from patients already on other SWOG protocols will be used. These protocols are: SWOG 9250, SWOG 9303, SWOG 9304, SWOG 9415, and SWOG 9420. Patient treatment will not be affected by registration on this protocol. TS expression will be measured using polymerase chain reaction. The following comparisons will be made: The relationship of TS expression (which may be the most important determinant of whether 5-FU will be effective) with tumor response in the disseminated setting and the relationship of TS expression with recurrence free survival in the post-operative adjuvant patients.

**Progress:** Five patients have been enrolled in this study at MAMC and continue to be followed. No patients were enrolled in FY 00.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 98/039

**Status:** Ongoing

**Title:** SWOG 9431: Cytogenetic, Molecular, and Cellular Biology Studies in Metastatic Melanoma Patients, Ancillary

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ Richard F. Williams, MC; MAJ Matthew P. Jones, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC

**Start Date:**

1/16/1998

**Est. Completion Date:**

Jul 01

**Periodic Review:**

1/25/2000

**Study Objective:** (1) To characterize the frequency of non-random cytogenetic abnormalities in regional and distant melanoma metastases (AJCC Stage III or IV) and explore their association with clinical outcome of melanoma patients enrolled onto Southwest Oncology Group trials; (2) to characterize the frequency of specific genetic alterations at either the DNA, mRNA, or protein level and explore the association of these abnormalities with clinical outcome in patients with regional and distant metastases (AJCC Stage III or IV) who are enrolled on Southwest Oncology Group melanoma trials. The specific genes to be studied in this protocol will initially include: p16 (MTS1), nm23; (3) to characterize the host immunologic response to metastatic melanoma by determining whether the in vitro pattern of cytokine expression is consistent with specific subsets of T helper cells (TH1 or TH2) within melanoma deposits. To explore whether host immunologic response varies based on the site of metastatic disease and/or correlates with clinical outcome in patients enrolled on Southwest Oncology Group trials; (4) To obtain peripheral blood, sera and paraffin embedded tumor blocks from patients with metastatic melanoma to create a tissue, cell and sera bank for future studies.

**Technical Approach:** Following informed consent, tissue and blood samples taken from biopsies will be sent to a special laboratory for storage and scientific testing.

**Progress:** No patients were enrolled in this study in FY 00.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 98/113	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9444: Gastrointestinal Tumor Repository Protocol, Ancillary		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC		
<b>Start Date:</b> 9/15/1998	<b>Est. Completion Date:</b> Apr 02	<b>Periodic Review:</b> 8/22/2000

**Study Objective:** 1) To establish a central gastrointestinal tumor repository to serve as a tissue resource for current and future scientific studies, 2) to utilize the Southwest Oncology Group clinical database to perform clinicopathologic correlation with the results of those studies, and 3) to test new hypotheses as they emerge.

**Technical Approach:** Tissue samples obtained during biopsies will be forwarded to a special laboratory for storage and scientific testing.

**Progress:** One patient was enrolled in the study in FY 98. No patients were enrolled in FY 00.

### Detail Summary Sheet

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<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/009	<b>Status:</b> Completed
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**Title:** SWOG 9457: Paclitaxel (Taxol) and Carboplatin for Advanced Transitional Cell Carcinoma of the Urothelium

**Principal Investigator:** MAJ David E. McCune, MC

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**Department:** SWOG

**Facility:** MAMC

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**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC

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**Start Date:**  
10/18/1996

**Est. Completion Date:**  
Nov 00

**Periodic Review:**  
9/28/1999

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**Study Objective:** 1) To assess the efficacy and feasibility of utilizing a 3 hour infusion of paclitaxel in combination with carboplatin in cases of previously untreated advanced urothelial tract transitional cell carcinoma. 2) To assess efficacy of this regimen with advanced urothelial tract transitional cell carcinoma refractory to platinum-based therapy. 3) To evaluate the toxicity of this regimen in these groups of patients.

**Technical Approach:** Advanced stage urothelial cancer that is not totally resected has a very high relapse rate. In fact in node positive disease it can be argued that these patients are incurable despite local resection. Of course M1 disease is incurable. Standard therapy for these tumors is cisplatin based (MVAC or CMV) with very good response rates in the 50 to 70 percent range. Phase II studies has seen response rates with single agent carboplatin in this range and Taxol single agent response rates in 25 to 30% range. This study is a Phase II study evaluating the efficacy of combined Carboplatin plus Taxol in patients with measurable advanced transitional cell carcinoma of the bladder.

**Progress:** This study closed to patient entry 1 Apr 00, when its accrual goal was reached. One patient was enrolled at MAMC, however the patient died Dec 97.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 97/041	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9510: Evaluation of Topotecan in Hormone Refractory Prostate Cancer, Phase II		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC		
<b>Start Date:</b> 12/19/1996	<b>Est. Completion Date:</b> Dec 00	<b>Periodic Review:</b> 11/19/1999

**Study Objective:** 1) To evaluate the response (CR and PR only) rate to topotecan in patients with metastatic, hormone-refractory prostate cancer. 2) To assess the qualitative and quantitative toxicities of topotecan administered in a phase II study to patients with metastatic, hormone-refractory prostate cancer.

**Technical Approach:** Prostate cancer that is refractory to standard first line hormonal manipulations including surgical and chemical orchiectomy has a median survival of about 6 months. The standard of care for hormone refractory prostate cancer is not defined. Response to chemotherapy is poor at about 10 to 15%. This study will assess the response rate and toxicities of Topotecan in hormone refractory prostate cancer patients. The schedule with a 21 day infusion had been tested at New York University and showed only some grade 3 and one grade 4 myelotoxicity. Other side effects are fatigue, nausea, vomiting and diarrhea.

**Progress:** This protocol closed to patient accrual 15 Aug 99. Three patients were enrolled in this study in FY 97 at MAMC and continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 96/095

**Status:** Ongoing

**Title:** SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC

**Start Date:**  
4/19/1996

**Est. Completion Date:**  
May 99

**Periodic Review:**  
3/28/2000

**Study Objective:** 1) To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen or progesterone receptors who are treated with standard adjuvant tamoxifen vs. tamoxifen and fenretinide; 2) to gain wider experience and toxicity information on the combination of tamoxifen and fenretinide; and 3) to obtain tumor tissue from these patients for future biologic studies of relevance to this patient population.

**Technical Approach:** The present standard of therapy for node positive and ER positive post menopausal women is Tamoxifen alone. There are some studies that suggest that the addition of adjuvant chemotherapy combined with hormonal therapy will prolong relapse free and overall survival. However, not all patients, especially in the over 65 year old age group, can tolerate or want the significant side effects of chemotherapy. Thus, a less toxic regimen is needed. This study attempts to use a chemoprophylactic approach along with the standard Tamoxifen treatment for this group of patients. This new retinoid has shown some effectiveness in Phase I and II studies when given in combination with Tamoxifen to untreated metastatic breast cancer patients. This study will test its use in a Phase III randomized, prospective, placebo-controlled trial. The side effects seem to be fairly minimal except for night blindness which will be closely monitored during this trial.

**Progress:** One patient enrolled in FY 97, three patients enrolled in FY 98 at MAMC. All four patients continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 96/118      **Status:** Completed

**Title:** SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; MAJ James S. D. Hu, MC; LTC Robert B. Ellis, MC; LTC Robert D. Vallion, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Steven S. Wilson, MC; MAJ Nyun C. Han, MC; CPT Brent L. Kane, MC; LTC Kenneth A. Bertram, MC

**Start Date:**  
5/17/1996

**Est. Completion Date:**  
Jun 00

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) To determine the efficacy of concurrent cisplatin and radiotherapy following surgical resection in patients who have advanced squamous cell carcinoma of the head and neck region; 2) to test whether the use of concurrent chemoradiotherapy following surgery increases locoregional control rates; 3) to determine if the patterns of first failure are changed by the use of concurrent chemotherapy; 4) to determine whether the use of concurrent chemoradiotherapy prolongs disease-free survival and/or overall survival; and 5) to compare the toxicity of concurrent chemoradiotherapy versus radiation alone in the postoperative setting.

**Technical Approach:** In head and neck squamous cell carcinomas with high risk features, there is a 20 to 50 percent recurrence rate after surgical resection. These high risk features include greater than 2 lymph nodes positive, extracapsular extension of cancer in lymph nodes, and positive resection margins. In the past, patients with these high risk features had received radiation therapy for local control. There is evidence, however, that the addition of cisplatin with concurrent radiation therapy may help in local control. This data comes from in vitro as well as in vivo data showing cisplatin may be a radiation sensitizer that may have synergistic local effects on malignancies. The study is a Phase III randomized study that will compare standard radiation therapy against concurrent cisplatin and radiation therapy for resected squamous cell carcinoma of the head and neck. The added toxicities of neuropathy, nausea and emesis, renal failure, and bone marrow suppression are tolerable and can be prevented with medical measures. It is hoped that local recurrence will be reduced with this approach with minimal added toxicity.

**Progress:** The study closed to patient entry 28 Apr 00, after reaching its accrual goal. One patient enrolled in this study in FY 96 at MAMC, but has been lost to follow-up.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/019	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9808: Long-Term Follow-Up Protocol: An Administrative Tool			
<b>Principal Investigator:</b> MAJ David E. McCune, MC			
<b>Department:</b> SWOG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC			
<b>Start Date:</b> 10/20/1998	<b>Est. Completion Date:</b> Indef		<b>Periodic Review:</b> 10/24/2000

**Study Objective:** To relieve the burden on Institutional Review Boards at Southwest Oncology Group Institutions for continuing review of protocols that are closed to patient registration, and on which no patients are currently receiving protocol treatment.

**Technical Approach:** When a study has been closed to patient accrual and patients have finished treatment, it still requires submission of data to the Southwest Oncology Group to report survival and remission status and occurrence of adverse events. On an annual basis, the Southwest Oncology Group Operations Office will notify the institutions as to which protocols are eligible for transfer to the Long Term Follow-Up protocol by periodically revising the list of applicable protocols. The institutional Principal Investigator or IRB will ultimately decide for the local institution whether the protocol should be included in this protocol or continue to be reviewed on its own. A report will be prepared and submitted for annual IRB review at individual institutions. This report will include title and date closed to patient entry.

**Progress:** This protocol includes consolidation of the following protocols at MAMC. All of the following protocols are closed to patient entry, the treatment phase is completed, and patients are being followed for survival data only: SWOG #s: 7406, 7433, 7436, 7510, 7713/14, 7808, 7827, 8216/38, 8269, 8313, 8410, 8417/19, 8516, 8600, 8736, 8809, 8892, 8957, 9019, 9125 and 9349

In FY 00, 2 patients on SWOG 8590 were included under this follow-up protocol

During FY '99, SWOG #s 8854, 9008, 9031 and 9445 were also consolidated.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 98/112		<b>Status:</b> Ongoing	
<b>Title:</b> SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma					
<b>Principal Investigator:</b> MAJ David E. McCune, MC					
<b>Department:</b> SWOG				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC					
<b>Start Date:</b> 9/15/1998		<b>Est. Completion Date:</b> Sep 02		<b>Periodic Review:</b> 8/22/2000	

**Study Objective:** (1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer, (2) to evaluate a panel of prognostic markers, in order to correlate these measures with survival and recurrence after adjuvant therapy in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer. The specific aims of the companion study will be: (a) to determine whether alterations in the expression of cell cycle related genes (thymidylate synthase, p53, and the cyclin-dependent kinase inhibitors p21 and p27) predict the risk of survival and recurrence in this patient population, (b) to determine whether alterations in markers of metastatic potential-expression of DCC and measures of tumor angiogenesis (microvascular density and vascular endothelial growth factor expression)-predict the risk of survival and recurrence in this patient population, (c) to determine whether a marker of cellular differentiation-sucrase isomaltase-predicts the risk of survival and recurrence in this patient population, and (d) to determine whether interactions among these tumor markers identify subsets of patients with significantly altered outcome.

**Technical Approach:** Subjects will be randomized and assigned to one of two treatment groups following standard surgical removal of their tumor. Group 1 will receive standard care which is surgery with no additional therapy after the tumor has been removed. Subjects will continue with routine check-ups, doctor visits and test. Group 2 will receive five antibody treatments using MoAb 17-1A. Subjects will receive the drug by as an intravenous infusion over a 2-hour time period once each 28 days. This 2-hour infusion will be repeated every 4 weeks for a total of 5 treatments. During treatment, various blood tests and x-rays will be used to determine whether the disease has returned

With subject's approval, tissue, body fluids, and other specimens obtained during the normal course of treatment will be forwarded to a special research laboratory for storage and scientific testing. Subjects will also be asked to complete a background information form to help define groups of patient being treated.

**Progress:** One patient enrolled in this study in FY 98 at MAMC and continues to be followed. No patients were enrolled in FY 00.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/037	<b>Status:</b> Ongoing
<b>Title:</b> SWOG C9732: A Randomized Phase III Study Comparing Etoposide and Cisplatin with Etoposide, Cisplatin and Paclitaxel in Patients with Extensive Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Jan 02	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether the addition of paclitaxel to standard chemotherapy treatment (etoposide/cisplatin) improves the survival of patients with extensive SCLC and to compare the tumor response rate and failure-free survival of patients with extensive SCLC who have received etoposide/cisplatin with or without paclitaxel and describe and compare the toxicities associated with etoposide/cisplatin treatment versus etoposide/cisplatin/paclitaxel treatment.

**Technical Approach:** This study compares two types of chemotherapy to determine the standard of care for extensive small cell lung cancer. Eligible patients will be randomized to receive one of two treatment regimens: Treatment 1 chemotherapy with etoposide and cisplatin or Treatment 2 chemotherapy with etoposide, paclitaxel and cisplatin

Treatment 1, patients will receive etoposide IV each day for 3 days and cisplatin, IV will be given with the first dose of etoposide. This treatment will be repeated every 21 days for a total of 6 treatment courses

Treatment 2, patients will receive paclitaxel and cisplatin, IV on day 1, and etoposide IV days 1-3. G-CSF will be started on days 4-18 to help blood cell counts to recover. This treatment will be repeated every 21 days for a total of 6 treatment courses.

**Progress:** No patients were enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/014      **Status:** Ongoing

**Title:** SWOG C9741: A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG      **Facility:** MAMC

**Associate Investigator(s):** LTC Kenneth A. Bertram, MC; MAJ Matthew P. Jones, MC

**Start Date:**  
12/15/1998

**Est. Completion Date:**  
Dec 01

**Periodic Review:**  
11/19/1999

**Study Objective:** (1) To compare sequential chemotherapy with Doxorubicin, Paclitaxel, and Cyclophosphamide to combined Doxorubicin and Cyclophosphamide followed by Paclitaxel for disease-free and overall survival, (2) to determine whether increasing the dose density of adjuvant chemotherapy (decreasing the interval between chemotherapy courses from 21 to 14 days) will improve disease-free and overall survival, and (3) to compare the toxicity for patients treated with sequential Doxorubicin, Paclitaxel, and Cyclophosphamide with toxicity for patients with concurrent Doxorubicin plus Cyclophosphamide followed by Paclitaxel at 14 and 21 day intervals.

**Technical Approach:** This is a randomized comparison of several aggressive combination chemotherapy regimens in the treatment of high-risk breast cancer due to positive lymph nodes. It compares the current standard of care for node positive breast cancer with several more aggressive variations. All patients will receive the same number of drugs and the same amount of drugs, but the order in which the drugs are given and the time between treatments (2 weeks versus 3 weeks) will be different. Arm 1, patients will receive Doxorubicin once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses followed by Cyclophosphamide once every 3 weeks x 4 total doses. Arm 2, patient will receive Doxorubicin once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses followed by Cyclophosphamide once every 2 weeks x 4 total doses. Arm 3, patients will receive Doxorubicin and Cyclophosphamide once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses. Arm 4, patients will receive patients will receive Doxorubicin and Cyclophosphamide once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses. G-CSF and Ciprofloxacin will be given concurrent with each arm to help ameliorate side effects of the treatments.

**Progress:** This study closed to patient accrual 31 Mar 99. Three patients were enrolled at MAMC in FY 99 and continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/036

**Status:** Ongoing

**Title:** SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
N/A

**Study Objective:** (1) To determine whether docetaxel improves disease-free survival and overall survival when compared to paclitaxel following 4 cycles of doxorubicin-cyclophosphamide therapy (2) To determine whether weekly administration of taxanes (paclitaxel or docetaxel) for 12 weeks improves disease-free survival and overall survival when compared with the conventional (every 3 weeks) schedule for 4 cycles following 4 cycles of doxorubicin-cyclophosphamide therapy (3) To compare the toxicity of docetaxel given weekly for 12 weeks to that of paclitaxel given every 3 weeks for 4 cycles (4) To compare the toxicity of paclitaxel given weekly for 12 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles (5) To compare the toxicity of paclitaxel given every 3 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles and (6) To compare the toxicity of paclitaxel given weekly for 12 weeks to that of docetaxel given weekly for 12 weeks.

**Technical Approach:** This study compares aggressive chemotherapy schedules to standard of care for high risk node positive breast cancer. Eligible patients will be randomized into one of four treatment arms: Arm A, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxol (the standard treatment); Arm B, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxol (lower dose than standard); Arm C, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxotere (medium dose); and Arm D, 12 weeks of adriamycin and cytoxan followed by 12 weeks of taxotere (low dose).

All Arms will receive adriamycin and cyclophosphamide, IV once every 3 weeks for 4 cycles. Then Arm A will receive taxol, IV once every 3 weeks for 4 treatments. Arm B will receive taxol IV once a week for 12 weeks of treatment. Arm C will receive Taxotere IV once every 3 weeks for 4 treatments. Arm D will receive taxotere once a week for 12 weeks of treatment.

**Progress:** Six patients have been enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/107      **Status:** Completed

**Title:** SWOG E1395: A Randomized Phase III Evaluation of Paclitaxel + Cisplatin Versus Cisplatin + 5-FU in Advanced Head and Neck Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
9/28/1999

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
N/A

**Study Objective:** To compare the efficacy and toxicity of Paclitaxel + Cisplatin with Cisplatin + 5-FU.

**Technical Approach:** Subjects will have a physical exam, blood tests, chest x-ray, and an EKG prior to being enrolled in this study and receiving treatment. These will be done to assess whether it is safe to administer treatment. After completion of initial studies subjects will be randomly assigned to one of two treatment arms: Paclitaxel + Cisplatin or Cisplatin + 5-FU. Treatment will be administered either in the hospital or as an outpatient. Before each cycle. Subjects will take 3 medications at 12 hours, 6 hours and 1 hour prior to receiving Paclitaxel to prevent any allergic reactions. These premedications include Decadron, Benadryl and Tagamet. Paclitaxel will be administered IV over 3 hours on day 1. On day 1 subjects will also receive Cisplatin, IV over 30 to 60 minutes. Prior to receiving the Cisplatin subjects will receive drugs to prevent nausea and vomiting. Intravenous fluids will be administered before, during and after the Cisplatin to help prevent kidney damage. This treatment will be repeated ever 3 weeks.

No matter which treatment arm a subject is on, they will see their doctor prior to each cycle for a physical exam and blood tests. This is considered routine for anyone receiving cancer treatment and will be used to monitor side effects. In addition, tumor measurements will be done at least every other cycle to determine their response to treatment. Subjects will continue on their treatment as long as your tumor is not growing. If at any time your tumor starts to grow, they will be taken off the study. The primary endpoint is overall survival at 1 year. Secondary endpoints include comparison of response rates and toxicity.

**Progress:** This protocol was reported closed to patient entry 12 Jan 00. No patients were enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/071		<b>Status:</b> Ongoing	
<b>Title:</b> SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytosan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer					
<b>Principal Investigator:</b> MAJ David E. McCune, MC					
<b>Department:</b> SWOG				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC					
<b>Start Date:</b> 5/25/1999		<b>Est. Completion Date:</b> Ape 03		<b>Periodic Review:</b> 4/25/2000	

**Study Objective:** To determine whether Adriamycin/Taxotere will improve disease-free survival and overall survival when compared to Adriamycin/Cytosan in lymph node positive (1-3 positive nodes) and high risk lymph node negative breast cancer. To compare toxicity of Adriamycin/Taxotere to Adriamycin/Cytosan.

**Technical Approach:** This is multi-site study with randomization to one of two arms: Adriamycin/Taxotere (AT) or Adriamycin/Cytosan (AC). The dosages for the AT group: Adriamycin 60 mg/M2 IV and Taxotere 60 mg/M2 IV over 1 hour infusion every 3 weeks x 4 cycles. Cipro 500 mg PO b.i.d. starting Day 8 and continuing x 10 days. If a patient is allergic to Cipro, an alternative broad spectrum antibiotic may be used. Decadron 8 mg PO b.i.d., beginning one day prior to treatment with Taxotere and continued for two additional days; repeat q 3 weeks x 4 cycles.

The dosages for the AC group: Adriamycin 60 mg/m2 IV and Cytosan 600 mg/ml IV. Every 3 weeks x 4 cycles.

In both groups, post-menopausal patients who are ER and/or PR positive will receive Tamoxifen 20 mg PO daily x 5 years at the completion of chemotherapy. G-CSF: Patients who have an episode of febrile neutropenia should be placed on G-CSF according to ASCO Guidelines. Patients who have febrile neutropenia after a subsequent dose of chemotherapy in spite of G-CSF should have the chemotherapy doses lowered by 25%.

**Progress:** This study closed to patient entry 21 Jan 00. One patient was enrolled in this study in FY 99 at MAMC and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/102	<b>Status:</b> Ongoing
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**Title:** SWOG E2697: Correlation of DNA Damage Index and Clinical Response in the Context of ECOG Trial E3695

**Principal Investigator:** MAJ David E. McCune, MC

<b>Department:</b> SWOG	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 03

**Periodic Review:**  
N/A

**Study Objective:** To determine, using an optimized DNA-PCR assay specific for exon-6 of the glutathione S-transferase (GST-TT, gene, the extent of cisplatin-induced DNA damage in vitro in PBMC obtained from melanoma patients prior to treatment with chemotherapy or biochemotherapy and correlate the extent of DNA damage with clinical response. To determine the optimum cisplatin concentration with which to treat PBMC in vitro that will provide the highest positive and negative predictive value for response to both chemotherapy and biochemotherapy.

**Technical Approach:** This study is a companion study to SWOG E3695. Patients will have blood drawn prior to receiving chemotherapy. The peripheral blood mononuclear cells will be exposed to different concentrations of cisplatin (one of the chemotherapy drugs in E3695). The amount of cisplatin induced DNA damage will be measured. The amount of damage will be compared to the response of the tumor to chemotherapy to see if there is a correlation.

**Progress:** This study has not yet received final IRB approval.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/056

**Status:** Ongoing

**Title:** SWOG E3695: A Randomized Phase III Trial of Concurrent Biochemotherapy with Cisplatin Vinblastine, Dacarbazine, IL-2, and Interferon A-2b versus Cisplatin, Vinblastine, Dacarbazine (CVD) Alone in Patients with Metastatic Malignant Melanoma

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Mar 01

**Periodic Review:**  
2/22/2000

**Study Objective:** 1) To determine whether this inpatient biochemotherapy is superior to CVD alone based on survival in patients with metastatic malignant melanoma. 2) To determine whether this inpatient biochemotherapy is superior to CVD alone based on response rate, response duration, time to treatment failure, percent CR and percent duration CR in patients with metastatic malignant melanoma. 3) To determine the feasibility of administering this in a biochemotherapy regimen to patients with metastatic malignant melanoma in a Cooperative Group setting. 4) To determine the toxicity of this inpatient biochemotherapy regimen relative to CVD alone in patients with metastatic melanoma treated in a Cooperative Group setting.

**Technical Approach:** Each subject will be randomized to one of two arms: Arm A (CVD): Treatment will consist of Cisplatin 20 mg/m<sup>2</sup> IV over 30 minutes. daily, days 1-4; Vinblastine 1.2 mg/m<sup>2</sup> IV daily, days 1-4; Dacarbazine 800 mg/m<sup>2</sup> IV over 1 hour, day 1 (only). Treatment can be administered in the outpatient setting. Cycles will be repeated every 3 weeks. Arm B (CVD + IL-2/IFN): Cisplatin 20 mg/m<sup>2</sup> IV over 30 minutes daily, days 1-4; Vinblastine 1.2 mg/m<sup>2</sup> IV daily, days 1-4; Dacarbazine 800 mg/ml FV over 1 hour, day 1 (only); IL-2 (Chiron) 9 MIU/m<sup>2</sup>/day by CIV, days 1-4 (96 hours); Interferon alpha 2b (Schering) 5MU/ml sc days 1-5, 8, 10 and 12; G-CSF 5 ug/kg sc qd days 7-16. All patients will be admitted to the hospital on the morning of day 1. Interferon alpha-2b, the IL-2 infusion and the rehydration for cisplatin should be planned to begin around 3 PM. Patients will be discharged ASAP after day 5 with subsequent doses of interferon to be administered in the outpatient setting or at home. Cycles will be repeated at 3 week intervals.

Tumor measurements will be obtained prestudy and tumor response will be assessed after every 2 cycles. Patients with stable or responding disease will continue on therapy until disease progression, unacceptable toxicity or until they receive the maximum of 4 cycles.

All patients will have renal function tests, blood counts and a thorough physical examination (including neurologic examination) prior to each cycle of chemotherapy. If abnormalities are found, these parameters will be rechecked on a weekly basis and further therapy will be withheld until laboratory values and performance status return to within the eligibility criteria (i.e., ANC > 1500/mm<sup>3</sup>, Platelets > 100,000/mm<sup>3</sup>, creatinine < 1.5, bilirubin < 1.5 and Performance Status 0 or 1).

**Progress:** No patients have enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00                      **Number:** 200/040                      **Status:** Ongoing

**Title:** SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG    **Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
1/25/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
N/A

**Study Objective:** (1) To compare CHOP treatment with or without chimeric anti-CD20 monoclonal antibody (IDEC-C2B8) in elderly patients with diffuse mixed, diffuse large cell, and immunoblastic large cell non-Hodgkin's lymphoma of B lineage with respect to response rate, the time to treatment failure, toxicity and survival, (2) To compare IDEC-C2B8 monoclonal antibody as maintenance therapy to observation alone after CHOP chemotherapy with respect to time to treatment failure, duration of response, toxicity and survival after an initial response to induction therapy of CHOP + IDEC-C2B8, and (3) To determine if maintenance therapy with IDEC-C2B8 results in the conversion of any partial responses to a complete response.

**Technical Approach:** This study adds a new drug, chimeric anti-CD20 monoclonal antibody, to the standard treatment (cyclophosphamide, doxorubicin, Vincristine and prednisone, CHOP) of Non-Hodgkin's Lymphoma. Patients eligible for this study will be randomized to receive or not to receive IDEC-C2B8 (anti-CD20) in conjunction with chemotherapy. Treatment Arm A, CHOP plus Anti-CD20 will receive the study drug IV over 6 to 12 hours on Days 7 and 3 before the first treatment cycle of CHOP. Anti-CD20 will also be given 48 hours prior to cycles 3, 5 and 7 of CHOP. Treatment Arm B will receive CHOP for a minimum of 6 or a maximum of 8 cycles. Restaging of disease after 4 cycles and again after 6 cycles will be done to determine response and eligibility to be randomized to Maintenance Treatment Arms C & D. Arm C will continue to receive Anti-CD20 IV, four weekly doses every 6 months for 2 years. Arm D will be the observation group.

**Progress:** Two patients enrolled in this study in FY 00 at MAMC.



### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 97/070

**Status:** Ongoing

**Title:** SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour .

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** LTC Robert L. Sheffler, MC; LTC Robert B. Ellis, MC; MAJ Richard F. Williams, MC; MAJ John R. Caton, MC; Rakesh Gaur, M.D.; LTC Kenneth A. Bertram, MC

**Start Date:**  
3/21/1997

**Est. Completion Date:**  
Mar 00

**Periodic Review:**  
2/22/2000

**Study Objective:** 1) To compare the duration of overall survival (OS) between completely rejected patients with T2 NO, T1-2N1 non-small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. 2) To determine disease-free survival. 3) To confirm the prognostic significance of ras mutations when present in the primary tumor. 4) To provide a comprehensive tumor bank linked to a clinical data base for the further study of molecular markers in rejected NSCLC. 5) To measure and compare health related quality of life in both treatment arms throughout the study period. 6) To evaluate toxicity related to chemotherapy.

**Technical Approach:** The role of adjuvant chemotherapy in Non-small cell lung cancer is controversial. Most clinical trials have shown no benefit to adjuvant chemotherapy. In the early 80's the lung cancer study group showed some benefit with combination chemotherapy in terms of survival, however, the control arm was not a strict observational arm and contained a "biological response modifier" in it. Thus with recent improved survival in Stage IV lung cancer shown compared to observation, it is assumed that using platinum based therapies may enhance survival in patients that have completely rejected non-small cell lung cancer. In patients with rejected Stage I, II, and III Non-small cell lung cancer it is known that the long term survival rates are 50 to 60%, 30 to 50%, and 19 to 49% respectively. It is thus the aim of this study to assess whether adjuvant therapy with Cisplatin and Vinorelbine will improve survival and relapse free survival compared to observation. In addition to the above study, tissue samples will be sent to the University of Washington for evaluation of Ras mutations to assess its prognostic importance.

**Progress:** One patient was enrolled in this study at MAMC in FY 00.

### Detail Summary Sheet

Date: 29 Sep 00	Number: 99/040	Status: Ongoing
Title: SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen		
Principal Investigator: MAJ David E. McCune, MC		
Department: SWOG	Facility: MAMC	
Associate Investigator(s): MAJ Matthew P. Jones, MC		
Start Date: 2/23/1999	Est. Completion Date: Jan 03	Periodic Review: 2/22/2000

**Study Objective:** Primary: To determine the disease-free survival and overall survival (all cause mortality) for women who have previously received  $\geq 5$  years of adjuvant tamoxifen, randomized to receive wither Letrozole 2.5 mg daily or placebo daily for 5 years.

Secondary: To evaluate the incidence of contralateral breast cancer. To evaluate the long term clinical and laboratory safety of Letrozole with special attention to: lipid profile as assessed by blood sampling (in a limited number of centers), cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) as assessed by reported toxicity, the incidence of all bone fractures (with particular emphasis on hip and wrist fractures as indicators of osteoporosis) as assessed by reported toxicity, changes in bone density (in a limited number of centers), common toxicities as assessed by reported toxicity.

Third: To evaluate overall quality of life.

**Technical Approach:** This is a multi-centre, double-blind, placebo-controlled parallel randomized trial of the NCIC Clinical Trials Group, supported by Novartis. Patients will be stratified by: receptor status at diagnosis (positive, unknown), lymph node status at diagnosis (negative, positive, unknown), and a prior adjuvant chemotherapy (yes, no). Patients will be centrally randomized to receive one of the following treatments: Arm 1 (letrozole): 2.5 mg po daily x 5 years or Arm 2 (Placebo): po daily x 5 years.

**Progress:** Four patients enrolled in FY 00, in addition to 3 patients enrolled in FY 99, for a total of 7 patients enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/121	<b>Status:</b> Ongoing
<b>Title:</b> SWOG N9741: A Randomized Phase III Trial of Combinations of Oxaliplatin (OXAL), 5-Fluorouracil (5-FU), and Irinotecan (CPT-11) as Initial Treatment of Patients with Advanced Adenocarcinoma of the Colon and Rectum		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC		
<b>Start Date:</b> 8/22/2000	<b>Est. Completion Date:</b> Aug 03	<b>Periodic Review:</b> N/A

**Study Objective:** 1) The primary objective is to compare the time to progression and overall survival in patients with locally advanced or metastatic colorectal cancer who receive one of these treatments: OXAL+5-FU+CF or CPT-11+OXAL or CPT-11+5-FU+CF (control regimen). 2) Secondary objectives include evaluation of toxicity, response rate, time to treatment failure and quality-of-life parameters in patients on the three regimens.

**Technical Approach:** This trial will compare the current standard of care for metastatic and locally advanced colon cancer to two promising new regimens. The goal is to define the new standard of care for this illness. Subjects will be randomized to receive one of three different treatments using two or three of the following 4 chemotherapy drugs: CPT-11, OXAL, 5-FU, and CF. The 3 different treatment schedules differ in the number of drugs and the amount of the drug you will receive, the amount of time over which the drugs will be given, and the length of cycles (time between doses). A complete physical to include labs, blood tests, scans and X-rays will be given at the beginning of each cycle. The 1st two cycles on the weeks you do not receive treatment, you will be contacted by telephone to talk about how you are feeling and if you are having any side effects. The treatments are as follows: Treatment A: CPT-11 will be given into a vein over 90 minutes followed by CF and 5-FU given into a vein over a few minutes, on day 1 for 4 of 6 weeks, repeated every 6 weeks. (A cycle is 6 weeks); Treatment F: OXAL will be given by vein over 120 minutes followed by CF given over 120 minutes followed by 5-FU (given over a few minutes of time) followed by 5-FU given over 22 hours. The CF and 5-FU are given on two consecutive days. Treatment is repeated every 14 days. This requires placement of an IV tube into a vein under the skin of the chest wall. Treatment G: OXAL will be given into a vein followed by CPT-11 over 30 minutes repeated every 3 weeks.

Subject will continue same treatment until disease fails to respond to the treatment. If a complete remission is obtained, treatment may be halted and reinitiated if cancer returns. To study the treatment's effect on quality of life, participants will be asked to fill out brief forms with questions about changes in daily routines and health. This will take about 10-15 minutes. The forms will be given to the participants during their visits to the clinic. If the participant is not feeling well enough to fill out the form, a copy will be given to the participant to take home. The participant will be called within the week to go over the questionnaires and get the answers. Family members or friends are not allowed to fill out the questionnaires for the participant. Because quality of life may change over time, the participant will be asked to fill out the same form a number of times during the study (before starting the first cycle of treatment, prior to cycle two, then before every other cycle of treatment, and after the last cycle of treatment).

**Progress:** This study has not yet received final IRB approval.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/120	<b>Status:</b> Ongoing
<b>Title:</b> SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel with or without Trastuzumab as Adjuvant Treatment for Women with HER-2 Overexpressing Node Positive Breast Cancer (an Intergroup Study)		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC		
<b>Start Date:</b> 8/22/2000	<b>Est. Completion Date:</b> Dec 05	<b>Periodic Review:</b> N/A

**Study Objective:** To see if the addition of Herceptin to standard AC + Taxol is beneficial for women with node positive breast cancer, whose tumors have excess amount of Her-2 gene.

**Technical Approach:** Subjects will have a full medical history and physical examination taken along with blood tests, chest x-ray, an electrocardiogram (a test that records the electrical activity of your heart), a MUGA or echocardiogram (a test that learns the function of your heart), a mammogram, and other tests that the doctor might feel are needed to fully learn about your disease. Subjects will be randomly assigned to one of three arms: Arm A - Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), Taxol by vein over 1 hour one day every week for a total of 12 treatments. Total length of treatment will be about six months. Arm B - Subjects will be given Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), you will get Taxol by vein over 1 hour one day every week for a total of 12 treatments. After all treatment with Taxol is done (about week 24), Herceptin by vein one day every week for one year. The first dose of Herceptin will be given over about 90 minutes. Subjects will be watched for 1 hour after the first dose of Herceptin. If they do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about 18 months. Arm C - Subjects will be given Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), subjects will be given Taxol, by vein over 1 hour, plus Herceptin, by vein one day every week, for a total of 12 treatments. After all treatment with Taxol plus Herceptin is done (about week 23), subjects will get Herceptin alone one day every week for six months. The first dose of Herceptin will be given over about 90 minutes. You will be watched for 1 hour after the first dose of Herceptin. If subjects do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about one year.

Regardless of which treatment, at the end of all chemotherapy, subject may also get tamoxifen, if estrogen or progesterone receptor positive, for five years. If subjects had a lumpectomy, they will also get radiation therapy after chemotherapy has ended. Blood samples will be taken before the start treatment for research use. Subjects will be followed indefinitely.

**Progress:** This study has not yet received final IRB approval.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/010	<b>Status:</b> Ongoing
<b>Title:</b> SWOG R9704: A Phase III Study of Pre and Post Chemoradiation 5-FU vs. Pre and Post Chemoradiation Gemcitabine for Postoperative Adjuvant Treatment of Resected Pancreatic Adenocarcinoma		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 10/26/1999	<b>Est. Completion Date:</b> Sep 02	<b>Periodic Review:</b> 10/24/2000

**Study Objective:** (1) To determine whether 5-FU based chemoradiation preceded and followed by gemcitabine improves the overall survival, local-regional and distant disease control, and/or disease free survival as compared to 5-FU based chemoradiation preceded and followed by 5-FU in the postoperative adjuvant a treatment of pancreatic carcinoma, (2) To compare the acute and late toxicities between 5-FU based chemoradiation preceded and followed by gemcitabine and 5-FU based chemoradiation preceded and followed by 5-FU and, (3) To prospectively evaluate the ability of post-resectional CA19-9 to predict survival among adjuvantly treated patients who have undergone a potentially curative resection for adenocarcinoma of the pancreas.

**Technical Approach:** This study compares two different approaches to reducing the risk of relapse after resection of pancreatic carcinoma. 5-FU plus radiation is given to both groups. Pre- and post-radiation chemotherapy is given using either 5-FU or Gemcitabine.

**Progress:** One patient was enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/072	<b>Status:</b> Completed
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**Title:** SWOG S9626: A Phase III Trial of Placebo Versus Megestrol Acetate 20 mg/Day Versus Megestrol Acetate 40 mg/Day as Treatment for Symptoms of Ovarian Failure in Women Treated for Breast Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC

**Start Date:**  
5/25/1999

**Est. Completion Date:**  
Apr 03

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) To compare the effectiveness and duration of the benefit of placebo and two dose levels of megestrol acetate in the reduction of severe and/or frequent hot flashes in patients with a history of adequate local and regional treatment of invasive breast cancer. 2) To document the effects, if any, of various dose levels of megestrol acetate on atrophic vaginitis and dyspareunia. 3) To evaluate the toxicity of two dose levels of megestrol acetate relative to placebo. 4) To evaluate the feasibility of accrual of patients to a placebo-controlled study evaluating megestrol acetate in patients with a history of invasive breast cancer which has undergone adequate local and regional treatment.

**Technical Approach:** Stage T1-3, N0-1, M0 infiltrating breast cancer treated with appropriate local and regional therapy; pts w/DCIS are not eligible; pts must have completed all primary therapy for breast cancer; pts taking tamoxifen must have started tamoxifen  $\geq$  4 months prior to randomization; pts must have never participated in any NCI sponsored adjuvant breast protocols; pts must have completed Patient Daily Log of Hot Flashes for 7 days prior to randomization and must have recorded 10 or more hot flashes of any severity or 5 or more severe or very severe hot flashes; pt must not be pregnant; pts must not currently be on steroids or any other hormones except tamoxifen.

**Progress:** This protocol closed to patient entry, 1 May 00, when the accrual goal was reached. No patients enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 99/073

**Status:** Ongoing

**Title:** SWOG S9700: A Phase II Trial of Infusional 5-Fluorouracil (5-FU), Calcium Leucovorin (LV), Mitomycin-C (Mito-C), and Dipyridamol (D) in Patients with Locally Advanced Unresected Pancreatic Adenocarcinoma

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC

**Start Date:**  
5/25/1999

**Est. Completion Date:**  
Mar 02

**Periodic Review:**  
4/25/2000

**Study Objective:** 1) The primary goal of this study is to assess the one-year overall survival rate in patients with advanced, unresectable pancreatic cancer who are treated with this regimen. 2) To assess the response rate in patients with measurable disease. 3) To evaluate the frequency and severity of toxicities associated with this therapy. 4) To assess the rate of resectability in patients who respond to this regimen.

**Technical Approach:** Stage II/III (based on AJCC Staging, Version 4) pancreatic adenocarcinoma not amenable to curative resection; PS 0-2; Meas or Eval disease; Histologically or cytologically proven ductal or undifferentiated adenocarcinoma (see protocol for acceptable histological types); No prior systemic CT/RT for pancreatic cancer; No other prior malignancy except adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I/II cancer from which patient is currently in complete remission, or any other cancer from which patient has been disease-free for 5 years;  $\geq 2$  weeks beyond any surgical bypass procedure & recovered from all surgical effects. A pancreatic primary cancer must be established by surgical exploration, CT scan or MRI. Patients who have unresected but localized disease are eligible (determined by total occlusion or encasement  $> 75\%$  of main portal vein or superior mesenteric vein, total occlusion of or  $> 75\%$  circumferential encasement of superior mesenteric artery, celiac axis or common hepatic artery, right or left hepatic arteries, total occlusion of peripheral splenic vein in patients without evidence of cirrhosis, tumor size of  $\geq 5$  cm involving body or tail of pancreas, or enlargement of celiac axis nodes with subsequent biopsy to prove pathologic involvement); Patients must not have lost  $> 15\%$  of actual body weight. (must have an oral intake of greater than 1,200 calories/day at time of registration); Pregnant/nursing women are ineligible.

**Progress:** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/092      **Status:** Completed

**Title:** SWOG S9714: Phase II Trial of Paclitaxel by 96-Hour Infusion in Stage IIIB and IV Bronchioloalveolar Carcinoma (BAC)

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
8/24/1999

**Est. Completion Date:**  
Aug 02

**Periodic Review:**  
N/A

**Study Objective:** 1) Assess the survival, progression-free survival and response rate in previously untreated patients with bronchioloalveolar carcinoma receiving intravenous paclitaxel by 96-hour continuous intravenous infusion. 2) Evaluate the side effects and overall toxicities of paclitaxel in 96 hour continuous infusion.

**Technical Approach:** All patients must have a biopsy-proven, incompletely resected or unresectable bronchioloalveolar carcinoma, Stage III B disease or Stage IV disease. Tumors may be multifocal or diffuse. Patients must have measurable or evaluable disease. All tests to assess measurable disease must have been performed within 28 days prior to registration. All tests to assess evaluable disease must have been performed with 42 days prior to registration. Patients must have a SWOG performance status of 0-2. All patients must not have received any prior chemotherapy, radiation therapy or biologics for lung cancer. All patients must have an alkaline phosphatase performed within 28 days prior to registration. No other prior malignancy is allowed except for the following: adequately treated basal cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease-free for five years. Patients with a history of brain metastases are not eligible for this study. Women/men of reproductive potential may not participate unless they have agreed to use an effective contraceptive method. The descriptive factors for this study are: Weight loss based on the six months prior to registration (<5% versus >5%), Stage IIIB vs Stage IV, and LDH normal ( $\leq$  ULN) versus abnormal ( $>$  ULN).

**Progress:** This study was permanently closed to patient entry 15 Mar 00, when it reached its accrual goal. No patients enrolled at MAMC.



### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 99/059      **Status:** Completed

**Title:** SWOG S9803: The Evaluation of Gemcitabine (Gemzar) in Resistant and Relapsing Multiple Myeloma, Phase II

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Mar 03

**Periodic Review:**  
N/A

**Study Objective:** 1) To evaluate the confirmed complete remission, remission and partial remission rate for refractory myeloma treated with gemcitabine. 2) To evaluate the qualitative and quantitative toxicities of gemcitabine administered in a Phase II study.

**Technical Approach:** Subjects will receive 1000 mg/m<sup>2</sup> Gemcitabine (IV over 30 minutes, days 1, 8, and 15 every 28 days) until the study ends (approximately March 2003). Subjects will have Gemcitabine discontinued if any of the following occur: progress of disease, unacceptable toxicity, subject requests withdrawal, delay of more than 3 weeks in protocol treatment due to toxicity. All patients will be followed until death.

**Progress:** This study was closed to patient entry 15 Dec 99. No patients enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/060	<b>Status:</b> Ongoing
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**Title:** SWOG S9806: Randomized Phase II Trial of Carboplatin/Gemcitabine Followed by Paclitaxel or Cisplatin/Vinorelbine Followed by Docetaxel in Advanced Non-Small Cell Lung Cancer

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC

**Start Date:**  
3/23/1999

**Est. Completion Date:**  
Mar 03

**Periodic Review:**  
2/22/2000

**Study Objective:** 1) Assess the survival and failure-free survival of patients with advanced non-small cell lung carcinoma treated with carboplatin and gemcitabine followed by paclitaxel or cisplatin and vinorelbine followed by docetaxel. 2) Evaluate the response (confirmed plus unconfirmed) and toxicities associated with these two regimens in this group of patients with advanced non-small cell lung cancer.

**Technical Approach:** Pts. must have histologically or cytologically proven new diagnosed selected Stage IIIB or IV advanced primary NSCLC (adenocarcinoma, large cell carcinoma, squamous cell carcinoma or unspecified) or recurrent disease after previous surgery and/or irradiation; pts. with brain mets are ineligible; pts. must have measurable or evaluable disease; pts. with bronchioloalveolar carcinoma or Stage IIIB tumor involving the superior sulcus (Pancoast Tumors) are ineligible; PS 0-1; at least three weeks must have elapsed since the completion of prior RT and surgery and pts. must have recovered from all associated toxicities; measurable or evaluable disease must be present outside the area of surgical resection; pts. must have a serum creatinine  $\leq 2 \times$  IULN and calculated or measured creatinine clearance  $\geq 50$  cc/min; pts. must not have rec'd prior hormonal, systemic or biologic therapy for NSCLC; pts must not receive concurrent hormonal, biologic or RT to measurable or evaluable lesions; pts. may receive concurrent palliative RT to small field non-measurable sites of disease (painful bony mets).

**Progress:** This study closed to patient entry 15 Nov 99. Two patients were enrolled in this study in FY 99 at MAMC and continue to be followed.

### Detail Summary Sheet

**Date:** 29 Sep 00      **Number:** 200/009      **Status:** Ongoing

**Title:** SWOG S9809: The Effect of Fluoroquinolones on the Disease-Free Interval in Patients with Stage Ta Transitional Cell Carcinoma of the Bladder, Phase III

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG      **Facility:** MAMC

**Associate Investigator(s):** MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; MAJ Raymond S. Lance, MC

**Start Date:**  
10/26/1999

**Est. Completion Date:**  
Sep 02

**Periodic Review:**  
N/A

**Study Objective:** To determine if ciprofloxacin improves the recurrence-free survival of patients with superficial transitional cell carcinoma of the bladder treated with a transurethral tumor resection (TURBT), to detect nonrandom cytogenetic changes in recurrent transitional cell carcinoma (TCC) of the bladder (specifically changes involving loss of chromosome 9 and gain of chromosome 7) and to correlate these cytogenetic changes with clinical-pathological indicators of tumor recurrence to cephalixin or Ciprofloxacin.

**Technical Approach:** Subjects will be randomized into one of two treatment groups; Arm 1, Ciprofloxacin for 3 days starting the night before the TURBT or Arm 2, Cephalixin for 3 days starting the night before the TURBT (if subjects are allergic to penicillin or a cephalosporin then sulfamethoxazole/trimethoprim for 7 days). Follow-up will be conducted for 5 years.

**Progress:** This protocol has not yet received final approval.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 99/038	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9832: Enhancing Well-Being During Breast Cancer Recurrence			
<b>Principal Investigator:</b> MAJ David E. McCune, MC			
<b>Department:</b> SWOG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC			
<b>Start Date:</b> 2/23/1999	<b>Est. Completion Date:</b> Feb 03		<b>Periodic Review:</b> N/A

**Study Objective:** To assess the effectiveness of a telephone intervention delivered by breast cancer survivors on well-being of patients experiencing a first recurrence of breast cancer, to examine the impact of sociodemographic, clinical, and psychosocial predictors of well-being in patients experiencing a first recurrence of breast cancer and to examine changes in well-being over time since recurrence.

**Technical Approach:** This is a randomized study with two arms: 1) standard institutional support or 2) intervention support by Y-ME. Intervention will be delivered by women who are particularly well-qualified to provide support and information: breast cancer survivors who have themselves experienced recurrence. Subjects will be asked to fill out several questionnaires. The questions asked are about how they are feeling and problems they've experienced related to their cancer. A peer counselor (a woman who has also had a recurrence of breast cancer) will be administering 4-8 questionnaires by phone over the course of 4 weeks for those in the intervention group. The subjects will also be asked to fill out a questionnaire 2 and 5 months after their last session. This data will be analyzed to determine if the intervention was helpful.

**Progress:** This protocol has not received final IRB approval; therefore, no patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/038	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9900: A Randomized Phase III Trial Surgery Alone or Surgery plus Preoperative Paclitaxel/Carboplatin in Clinical Stage IB (T2N0), II(T1-2N1, T3N0) and Selected IIIA (T3N1) Non-Small Cell Lung Cancer (NSCLC)		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Jan 00	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To assess whether preoperative chemotherapy with paclitaxel and carboplatin for 3 cycles improves survival compared to surgery alone in previously untreated patients with clinical Stage IB, II and Selected III A non-small cell lung cancer (NSCLC), (2) To compare operative mortality and other toxicities in the two study arms, (3) To evaluate the response rates (confirmed and unconfirmed, complete and partial) and the toxicities associated with the combination of paclitaxel and carboplatin, and (4) To obtain samples for correlation of radiologic, pathologic, molecular and biologic factors with outcome.

**Technical Approach:** This study compare surgery (the standard therapy) to chemotherapy followed by surgery to determine the standard of care for non-small cell lung cancer (NSCLC). Patients will be randomized to either surgery alone or chemotherapy (paclitaxel, IV, Day 1 every 3 weeks; carboplatin, IV, Day 1 every 3 weeks) for nine weeks prior to surgery. Chest x-rays and CT scans will be repeated to determine response to the chemotherapy and decide when the surgery should be scheduled.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/119

**Status:** Ongoing

**Title:** SWOG S9901: A Randomized Phase III Trial Comparing Early High Dose Chemotherapy and an Autologous Stem Cell Transplant to Conventional Dose ABVD Chemotherapy for Patients with Advanced Stage Poor Prognosis Hodgkin's Disease as Defined by the International Prognostic Factors Project on Advanced Hodgkin's Disease, Intergroup

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Ines J. Sanchez-Rivera, MC; MAJ Patrick Williams, MC

**Start Date:**  
8/22/2000

**Est. Completion Date:**  
Aug 03

**Periodic Review:**  
N/A

**Study Objective:** 1) To compare in a cooperative group setting the progression-free survival in patients with poor prognosis advanced stage Hodgkin's disease who are treated with induction chemotherapy (ABVD X 5) followed by randomization to ABVD x 3 versus ABVD x 1 plus high dose chemotherapy plus peripheral blood stem cell rescue. 2) To compare the overall survival in this cohort of patients. 3) To compare the toxicities of these treatment regimens.

**Technical Approach:** This study will attempt to define the role of high dosed chemotherapy with stem cell transplant in the initial treatment of Hodgkin's Lymphoma. The study compares the standard of care (eight cycles of ABVD), to six cycles followed by high dose chemotherapy. Madigan expects to enroll 2 to 3 subjects per year.

**Progress:** This study has not yet received final IRB approval.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/082

**Status:** Ongoing

**Title:** SWOG S9902: Evaluation of the Combination of Docetaxel (Taxotere)/Carboplatin in Patients With Metastatic or Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN), Phase II

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Mar 03

**Periodic Review:**  
N/A

**Study Objective:** (1) To assess the survival in patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) when treated with the combination of Docetaxel (Taxotere®) and carboplatin plus dexamethasone, (2) To assess time until treatment failure and response rate (unconfirmed and confirmed complete and partial response), and (3) To evaluate the toxicities of this regimen.

**Technical Approach:** This study will try to determine the response rate of metastatic head and neck cancer to the combination of docetaxel and carboplatin. Subjects will be treated on an outpatient or possible inpatient. Docetaxel will be given IV over a period of 1 hour and carboplatin given IV over a period of 1/2 hour. In addition, subjects may also receive dexamethasone, IV over 30 minutes prior to docetaxel. This treatment will be repeated every 3 weeks as long as their disease stays the same or improves. Subjects will discontinue treatment if their disease progresses.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 99/108	<b>Status:</b> Completed
<b>Title:</b> SWOG S9911: A Phase II Pilot Trial of CHOP Followed by Iodine-131-Labeled Monoclonal Anti-B1 Antibody for Treatment of Newly Diagnosed Follicular Non-Hodgkin's Lymphomas		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC; LTC Marc G. Cote, MC		
<b>Start Date:</b> 9/28/1999	<b>Est. Completion Date:</b> Sep 02	<b>Periodic Review:</b> N/A

**Study Objective:** 1) To estimate the two-year failure-free survival rate of patients with newly diagnosed follicular lymphoma (CD20+) treated with six cycles of CHOP chemotherapy followed by Iodine-131 anti-B1 antibody. To estimate the response rate (confirmed and unconfirmed and unconfirmed complete and partial responses) for patients with newly diagnosed follicular lymphoma (CD20+) treated with this regimen. 3) To evaluate the toxicity of CHOP followed by Iodine-131 anti-B1 antibody in patients with newly diagnosed follicular lymphomas. 4) To estimate the rate of disappearance of cells with clonal t(14;18)/bcl2 rearrangements from the peripheral blood and bone; marrow after CHOP and iodine-131 anti-B1 antibody.

**Technical Approach:** Monoclonal antibodies can combine with standard chemotherapy often with low additional toxicity. This trial will establish the response rate of monoclonal antibody added to standard therapy for Non-Hodgkin lymphoma. This is an aggressive study in what has traditionally been a poor prognosis diseased.

**Progress:** This protocol closed to patient entry, 1 Jun 00. No patients were enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/039	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9914: Phase II Trial of Paclitaxel, Carboplatin and Topotecan with G-CSF in Untreated Patients with Extensive Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Matthew P. Jones, MC; MAJ Ines J. Sanchez-Rivera, MC		
<b>Start Date:</b> 1/25/2000	<b>Est. Completion Date:</b> Jan 00	<b>Periodic Review:</b> N/A

**Study Objective:** (1) Assess the survival of patients with extensive small cell lung cancer (SCLC) treated with a combination of paclitaxel, carboplatin and topotecan plus G-CSF, (2) Assess response rates of patients with extensive small cell lung cancer (SCLC) treated with a combination of Taxol, carboplatin and topotecan plus G-CSF, and (3) Evaluate the side effects and overall toxicities associated with the combination of paclitaxel, carboplatin and topotecan plus G-CSF.

**Technical Approach:** Eligible patients will receive the combination of three active chemotherapy drugs, carboplatin, paclitaxel and topotecan for the treatment of extensive small cell lung cancer. Topotecan IV will be given on days 1-4, and carboplatin IV and paclitaxel IV on day 4. Day 5, patients will begin G-CSF as a subcutaneous injection to help blood counts recover. This treatment will be repeated every 3 weeks for a total of 6 cycles.

**Progress:** No patients were enrolled in this study in FY00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00		<b>Number:</b> 200/083	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9916: Docetaxel and Estramustine versus Mitoxantrone and Prednisone for Advanced, Hormone Refractory Prostate Cancer, Phase III			
<b>Principal Investigator:</b> MAJ David E. McCune, MC			
<b>Department:</b> SWOG		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC			
<b>Start Date:</b> 5/23/2000	<b>Est. Completion Date:</b> Mar 03		<b>Periodic Review:</b> N/A

**Study Objective:** (1) To compare overall survival and progression-free survival in patients with hormone refractory metastatic prostate cancer Stage D1 or D2 (with either measurable or non-measurable disease) randomized between Arm 1 (docetaxel (Taxotere®), estramustine (Emcyt®)) and Arm 2 (mitoxantrone (Novantrone®) and prednisone), (2) To compare qualitative and quantitative toxicity between the two study arms, (3) To evaluate elements of Quality of Life, including: a. Palliation of metastatic bone pain and b. Global Quality of Life, (4) To record PSA values for future correlations with response and survival, and (5) To compare responses between the two treatment groups in patients with BioDimensional measurable disease.

**Technical Approach:** Subjects will be randomized to received either Treatment Arm 1, Docetaxel and Estramustine or Treatment Arm 2, Mitoxantrone plus Prednisone. Subjects in Arm 1 will receive estramustine as 2 capsules by mouth 3 x every day for 5 days plus a steroid medication by mouth on the 1st and 2nd days to decrease side effects of the docetaxel treatment. Docetaxel will be given IV on the 2nd day of the treatment course. This treatment procedure will be repeated every three weeks. Subjects in Arm 2 will receive mitoxantrone plus prednisone, by mouth twice every day for 3 weeks. The mitoxantrone treatment will be given on the 1st day, IV. This treatment procedure will be repeated every three weeks. All subjects will be asked to complete questionnaires on a regularly scheduled basis to describe the effect on their quality of life while receiving their specific treatments.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

**Date:** 29 Sep 00

**Number:** 200/084

**Status:** Ongoing

**Title:** SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III

**Principal Investigator:** MAJ David E. McCune, MC

**Department:** SWOG

**Facility:** MAMC

**Associate Investigator(s):** MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
5/23/2000

**Est. Completion Date:**  
Jan 02

**Periodic Review:**  
N/A

**Study Objective:** This study will evaluate overall survival using adjuvant systemic therapy in high risk localized prostate cancer patients following radical prostatectomy. Disease-free survival will also be evaluated. Patients will be randomized to one of the following two treatment arms: (A) Casodex, + Zoladex, (B) Novantrone/Prednisone followed by Casodex, + Zoladex. This study will also compare qualitative and quantitative toxicity between the two study arms.

**Technical Approach:** This study compares standard hormonal therapy after prostate cancer surgery to standard therapy plus chemotherapy to determine the best way to prevent relapse. Subjects will be randomized to receive either Treatment 1, Hormonal Therapy which consists of Zoladex, subcutaneous injection once every 12 weeks for two years or Treatment 2, Hormonal Therapy plus Mitoxantrone plus Prednisone which consists of Zoladex subcutaneous injection once every 12 weeks for two years, Casodex taken orally once a day for two years, Mitoxantrone, IV once every 21 days for 126 days (6 cycles) and Prednisone, taken orally twice a day for 126 days. Following study completion, subjects will be followed every 6 months for two years to assess response.

**Progress:** No patients were enrolled in this study in FY 00 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/101	<b>Status:</b> Ongoing
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**Title:** SWOG S9922: A Phase III Trial of Dexamethasone, Cyclophosphamide, Etoposide, Cisplatin (DCEP) and G-CSF with or without Thalidomide (NSC #66847) as Salvage Therapy for Patients with Refractory Multiple Myeloma

**Principal Investigator:** MAJ David E. McCune, MC

<b>Department:</b> SWOG	<b>Facility:</b> MAMC
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**Associate Investigator(s):** MAJ Ines J. Sanchez-Rivera, MC

**Start Date:**  
6/27/2000

**Est. Completion Date:**  
Jun 04

**Periodic Review:**  
N/A

**Study Objective:** 1) To evaluate and compare the overall and progression-free survival and confirmed remission rates in patients with refractory multiple myeloma treated with the DCEP regimen alone versus DCEP plus thalidomide. 2) To evaluate the qualitative and quantitative toxicities associated with these regimens.

**Technical Approach:** Most patients with multiple myeloma, even those treated with bone marrow transplant eventually relapse. There is no standard therapy for these patients. Combination chemotherapy and thalidomide have demonstrated activity against relapsed myeloma. This trial tests whether the addition of thalidomide to combination chemotherapy provides additional benefit.

**Progress:** This study has not yet received final IRB approval.

### Detail Summary Sheet

<b>Date:</b> 29 Sep 00	<b>Number:</b> 200/113	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9927: Randomized Trial of Post-mastectomy Radiotherapy in Stage II Breast Cancer in Women with One to Three Positive Axillary Nodes, Phase III		
<b>Principal Investigator:</b> MAJ David E. McCune, MC		
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Ines J. Sanchez-Rivera, MC; MAJ John B. Halligan, MC		
<b>Start Date:</b> 7/25/2000	<b>Est. Completion Date:</b> Jul 03	<b>Periodic Review:</b> N/A

**Study Objective:** To compare overall and disease-free survival in pre-and post-menopausal women with Stage II breast cancer and 1-3 positive nodes treated with or without radiation therapy following mastectomy and adjuvant chemotherapy. 2) To assess loca-regional control for this cohort of patients. 3). To assess the potential toxicities of radiotherapy delivered using CT-directed treatment in this cohort of patients.

**Technical Approach:** Current standard of practice does not include radiation therapy for patients with 1 - 3 positive nodes, but older studies suggest a benefit. This study will determine whether adding radiation therapy to modern chemotherapy will improve overall survival.

**Progress:** This study has not yet received final IRB approval.

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